Dissertation on

"STUDY ON PREVALENCE OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE"

Submitted in partial fulfillment for the Degree of

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CERTIFICATE

This is to certify that the dissertation entitled "**STUDY ON PREVALENCE OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE"** is a bonafide original work done by **Dr. SIVASUBRAMANIAN. B**, in partial fulfillment of the requirements for M.D. GENERAL MEDICINE BRANCH – I examination of the Tamilnadu Dr.M.G.R. Medical University to be held in April 2016, under my guidance and supervision in 2015.

Prof. S.G.SIVACHIDAMBARAM M.D.,
Guide and Supervisor,
Professor of Medicine,
Institute of Internal Medicine,
Madras Medical College & RGGGH,
Chennai – 600003

Prof. K.SRINIVASA GALU M.D.,
Director,
Professor of Medicine,
Institute of Internal Medicine,
Madras Medical College & RGGGH,
Chennai – 600003

Prof. R. VIMALA M.D.,
Dean
Madras Medical College &
Rajiv Gandhi Government General Hospital,
Chennai – 600 003.

DECLARATION BY THE CANDIDATE

I hereby solemnly declare that the dissertation entitled "**STUDY ON PREVALENCE OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE"** is done by me at Institute of Internal Medicine, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai during 2015 under the guidance and supervision of **Prof. S.G. SIVACHIDAMBARAM M.D.,** This dissertation is submitted to The Tamilnadu Dr. M.G.R Medical University, Chennai towards the partial fulfilment of requirement for the award of M.D. Degree in General Medicine (Branch I)

Place:

Date:

Dr. SIVASUBRAMANIAN. B

Post graduate student,

M.D. General Medicine,

Institute of Internal Medicine,

Madras Medical College & RGGGH,

Chennai – 600 003.

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CONTENTS

ABBREVATIONS

ABG – Arterial Blood Gas

ACE – Angiotensinogen Converting Enzyme

AF – Atrial Fibrillation

BMI – Body Mass Index

CAD – Coronary artery disease

CAT – COPD Assessment Test

COPD – Chronic Obstructive Pulmonary Disease

DT – Deceleration time

FEV_1 – Forced Expiratory Volume in one second

FVC – Forced Vital Capacity

GOLD – Global initiative of chronic Obstructive Lung Disease

HIF-1 – Hypoxia inducible factor-1

HRCT – High Resolution Computed Tomography

HRQOL – Health Related Quality of Life

ICS – Inhalational Corticosteroids

IHD – Ischemic Heart Disease

IVRT – Isovolumetric relaxation time

LABA – Long acting Beta 2 agonists

LAMA – Long acting antimuscarinic agents

LTOT – Long term oxygen therapy

LA – Left atrium

LV – Left Ventricle

LVRS – Lung volume reduction surgery

mMRC – modified Medical Research Council

PaO_2 – Partial pressure of oxygen

PDE- 4 – Phosphodiesterase 4

QOL – Quality of Life

RA – Right Atrium

RA – Right Ventricle

RVH – Right Ventricular Hypertrophy

SABA – Short acting beta2 agonists

SAMA – Short acting antimuscarinic agents

SaO_2 – Saturation of oxygen

TNF-α – Tumour Necrosis Factor- α

INTRODUCTION

INTRODUCTION

Chronic Obstructive Pulmonary Disease, a very common disease, and it is the 4th leading cause of death in worldwide. In India, it is the 2nd most common lung disorder after pulmonary tuberculosis. It is one of the preventable and treatable disease. Smoking and air pollution are the main risk factors.

COPD is a systemic disease, because inflammation is not only involved in lung airways, but also seen in systemically. So COPD is associated with variety of extra pulmonary manifestations. Most important systemic manifestation is Cardiovascular diseases, which are more frequently common in patients with COPD, and it is responsible for high mortality and morbidity. Among COPD patients, Cardiovascular disease is responsible for 50% of hospitalization and 20% of deaths.

Inflammation is one of the systemic manifestations of COPD and provides a hypothesis to explain the relationship between cardiovascular risk and airflow limitation. COPD increases the risk of cardiovascular disease regardless of age, sex, smoking status.

COPD is well known disease that can cause greater effect on right sided heart due to development of pulmonary hypertension. Cor pulmonale and right heart failure are the usual manifestations. But COPD increases the risk of developing other Cardiovascular manifestations are Ischemic Heart Disease, congestive heart Failure, arrhythmias, most commonly AF, etc.

Recent studies show that there is high prevalence Left Ventricular Diastolic Dysfunction is COPD patients even in the absence of ischemic heart disease. Diastolic heart failure prolongs the hospitalization and increases the risk of morbidity and mortality in COPD patients.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

- To assess the left ventricular diastolic function in COPD patients using Echocardiogram.

- To detect the presence of left ventricular diastolic dysfunction in all stages of COPD (GOLD Stages).

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Chronic obstructive pulmonary disease and its components has been known to humans for over 200 years. First, Bonet described the COPD as "voluminous lungs" in 1679 and Morgagni reported cases of "turgid" lungs in 1769.[1]

In 1984, Badham (British Physician) identified bronchiolitis and chronic bronchitis and he used the term 'catarrh' that indicates chronic inflammation of the mucous membrane.[2]

Laennec (the physician and inventor of the stethoscope) described "emphysema" in his *Treatise of diseases of the chest* in 1821. He recognized that emphysema lungs were excessively inflated.[3]

In 1846, John Hutchinson invented the spirometer, and that device measured vital capacity and In 1947, Robert Tiffeneau introduced the concept of timed vital capacity and created complete diagnostic spirometer.[4]

Oswald explained the clinical features of chronic bronchitis in 1953. Barach and Bickerman wrote the first comprehensive text book of "*Pulmonary emphysema"* in1956 and also described about the treatment. [5]

In 1976, Charles Fletcher wrote about the natural history of COPD and also indentified the link between smoking the accelerated rate of decline in lung function.[6]

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

COPD is the disease of airflow limitation which is not fully reversible which includes

1. Emphysema
2. Chronic bronchitis

DEFINITION OF CHRONIC BRONCHITIS (by British Medical Research Council)

Chronic bronchitis is defined as "Daily productive cough for at least three consecutive months for more than two successive years".[7]

DEFINITION OF EMPHYSEMA (by National Heart, Lung and Blood Institute in 1984)

Emphysema is a condition of the lung which is characterized by "abnormal, permanent enlargement of airspaces distal to the terminal bronchiole, accompanied by the destruction of their walls, and without obvious fibrosis"[8]

GOLD definition of COPD

COPD is a common preventable and treatable disease, characterized by "persistent airflow limitation, that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patient".[9]

EPIDEMOLOGY

- COPD – 2nd most common lung disorder after tuberculosis in India
- More common in middle aged patients. Rare below age of 35
- Equally prevalent in rural and urban areas
- Prevalence at global level is approximately 9-10%[10]
- In India prevalence is 3.49%[11]

RISK FACTORS

Genetic factors:

Alpha1-antitrypsin deficiency – strongest genetic factor for development of COPD.[12] Alpha 1-antitrypsin is a major circulating serine protease inhibitor, which is produced by liver.

Other genes related to development of COPD are [13]

- Alphanicotinicacetylcholine receptor
- Hedgehog-interacting protein gene
- *FAM13* gene
- Gene encoding MMP12

Environmental factors

Tobacco smoking is the main etiological risk factor for obstructive pulmonary disease[14].

Other environmental factors, which increase the risk of COPD are

- occupational exposure to dusts and fumes
- outdoor air pollution[16]
- exposure to biomass smoke
- second-hand smoke inhalation[23]

Adult cigarette smokers have following effects while comparing with non-smokers[17]

- have high risk respiratory infections and symptoms
- greater loss of lung density
- a greater reduction rate of FEV_1
- greater mortality rate

Infections and exacerbations

Recurrent severe respiratory infections in childhood usually associated with increased risk of COPD in adulthood.[18]

In established COPD, recurrent infections and exacerbations can lead to progression of disease and excessive decline in FEV_1[19]

Tuberculosis also one of the risk factor for COPD, mainly due to airflow limitation from scarring.[20]

Asthma and Bronchial Hyperreactivity

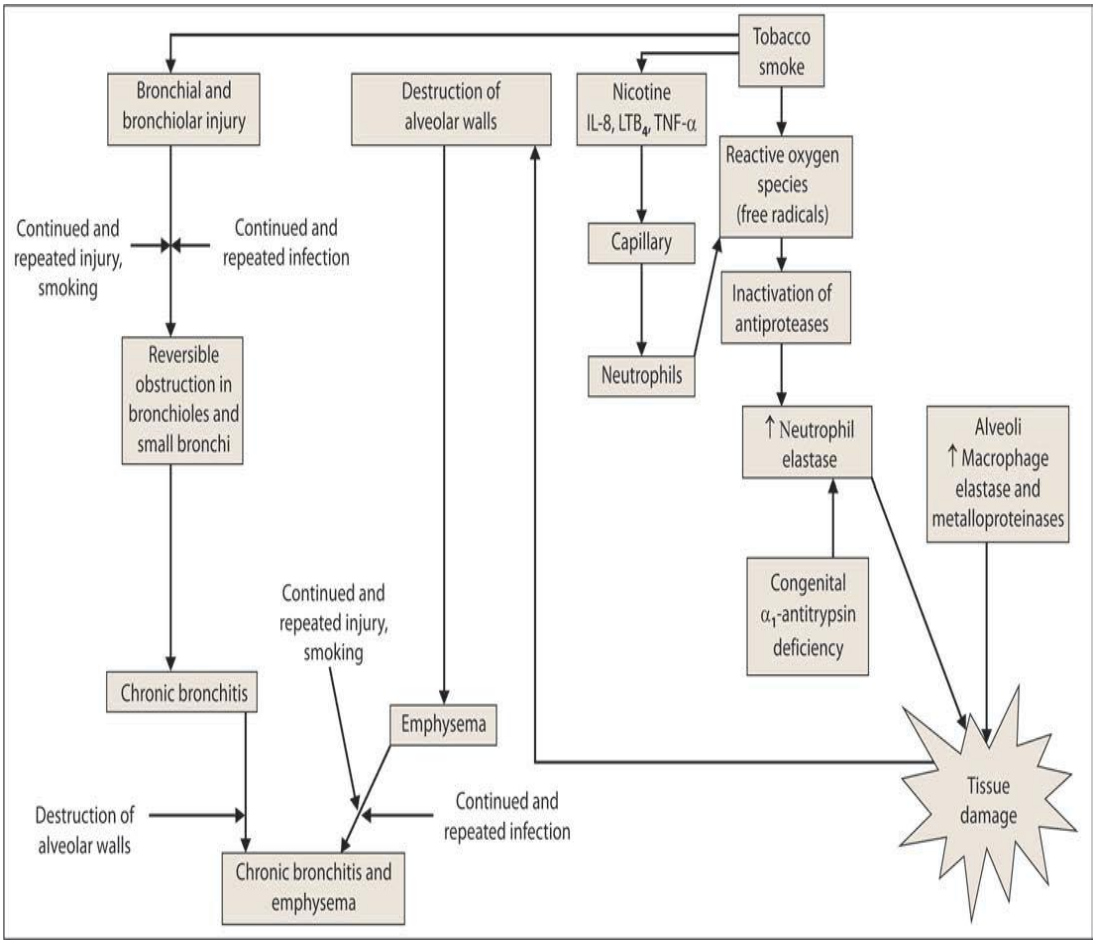
COPD and Asthma are the two different diseases with variable overlap. Asthma may be also one of risk factor for development of COPD.

Patients with asthma have 12 fold higher risk for occurring COPD.

PATHOGENESIS

There are multiple mechanisms involved in pathogenesis of COPD. Following theories are proposed in COPD.[21]

- proteinase-antiproteinase hypothesis
- immunological mechanisms
- oxidant-antioxidant balance[25]
- systemic inflammation[27]
- apoptosis and ineffective repair[26]



Pathogenesis of COPD and CHRONIC BRONCHITIS

PATHOLOGY

Cigarette smoking affects large airways, small airways(<2mm) and alveoli.

In COPD - major site of obstruction is small airways[24]

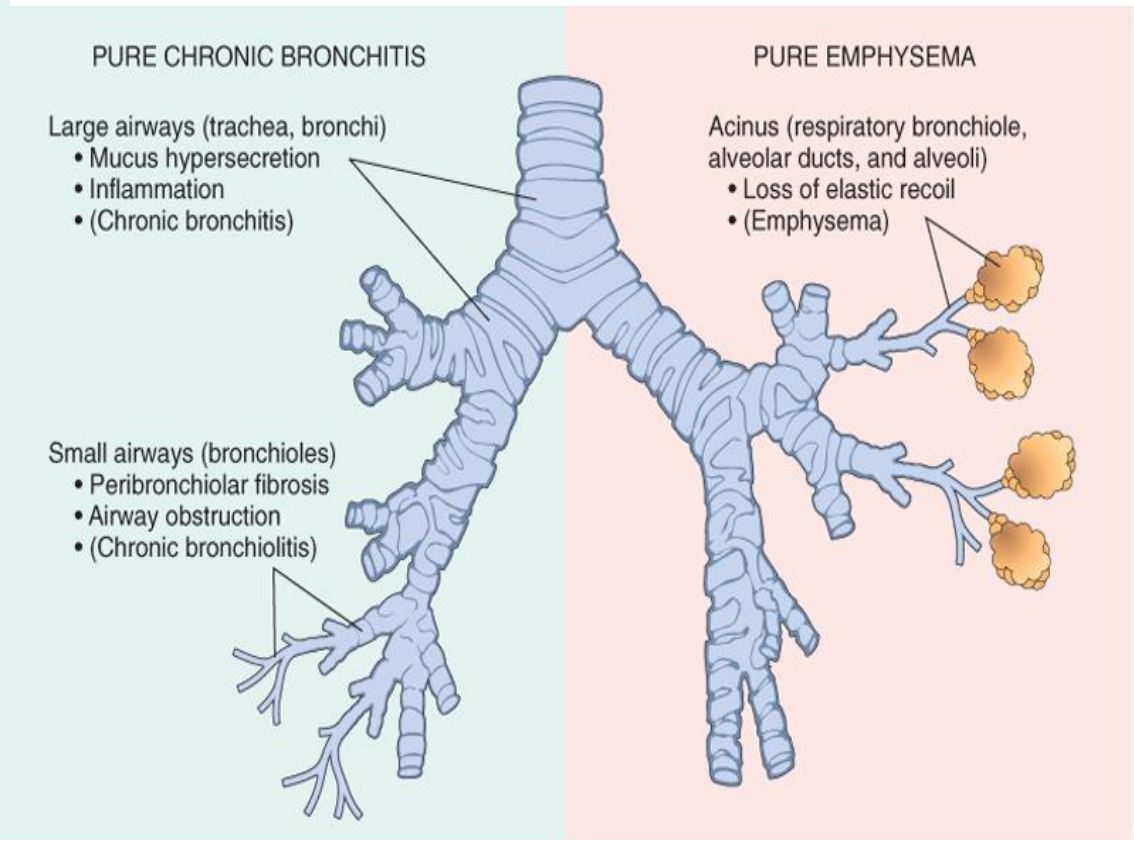
Chronic bronchitis

- hypertrophy of mucus secreting glands and goblet cell hyperplasia in large airways
- Reid index increases to 0.52 (normal 0.44)
- Reid index is defined as "ratio of thickness of submucosal glands to that bronchial wall"
- involvement small airways (chronic bronchiolitis) – major site of increased resistance in COPD

Emphysema

Destruction of alveoli, alveolar ducts and respiratory bronchioles, which are the gas exchanging air spaces, lead to decrease the lung elastic recoil, that results in reduction of maximal expiratory airflow.

Figure 1. Pathology of Chronic Bronchitis and Emphysema



PATHOLOGICAL FEATURES OF COPD

- Destruction of alveolar tissue and small airways
- Airway wall inflammation
- Edema and fibrosis[28]
- Intraluminal mucus

PATHOLOGICAL TYPES OF EMPHYSEMA

Centriacinar:

- Involves proximal part of acini (respiratory bronchiole)
- Associated with cigarette smoking
- Upper lobes and superior segments of lower lobes are more commonly involved.

Panacinar:

- Uniformly enlarged all part of acini from respiratory bronchiole to alveoli
- Common in Alpha1-antitrypsin deficiency
- Predominantly occurs in lower lobes.

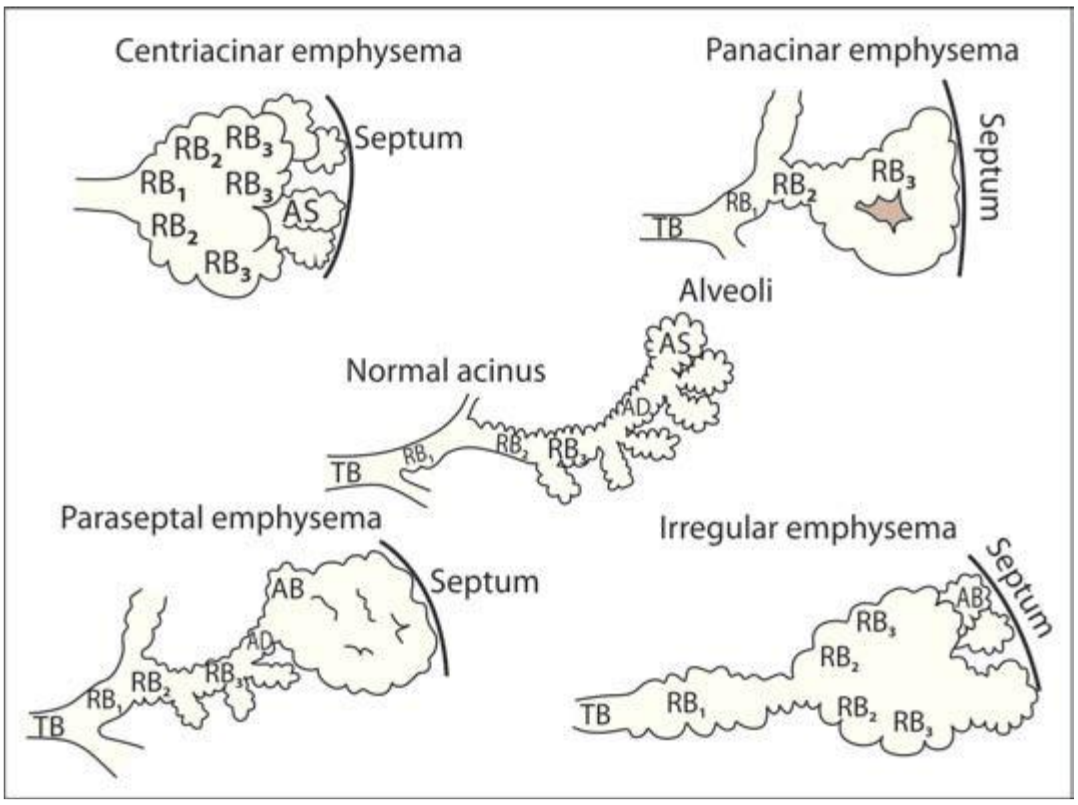
Paraseptal:

- Involves distal portion of acini (sparing of proximal portion)
- Usually occurs adjacent to pleura
- Progressive enlargement to form bullae
- More prone to spontaneous pneumothorax

Irregular emphysema:

- Irregular involevement of acini and almost always associated with scarring
- This pattern common in Tuberculosis.

Figure 2. Pathological types of emphysema



PATHOPHYSIOLOGY

Airflow limitation and air trapping:

- The extend of pathological changes in small airways is strongly interrelated with FEV_1 and FEV_1/FVC ratio
- Accelerated reduction in FEV_1 – characteristic of COPD[29]
- Hyperinflation of lungs occur as result of progressive trapping of air in the peripheral airways during expiration
- Hyperinflation leads to decrease in inspiratory capacity and also increases functional residual capacity, Tidal volume especially during exercise (also called dynamic hyperinflation) which results in progressive dyspnea and limitation of physical activity

Gas Exchange abnormalities: [30]

- Hypoxemia
- Hypercapnea

  Usually occurs in late stages of COPD (FEV_1 <50%)

CLINICAL FEATURES:

3 cardinal symptoms are

- Cough

- Sputum production
- Exertional dyspnea

PHYSICAL FINDINGS

- Early stages – normal physical finding
- Nicotine stain on fingernails (current smokers)
- Barrel shaped chest (sign of hyperinflation)
- Working accessory muscles
- Sitting in tripod position (to facilitate actions of sternocleidomastoid, scalene, intercostal muscle) – characterisitic position
- Patients with emphysema are called Pink puffers , they are thin and non-cyanotic at rest, and prominent action of accessory muscles
- Blue bloaters – heavy and cyanotic (Chronic Bronchitis)
- Expiratory wheeze on auscultation

Sings of advanced disease:

- Cachexia[22]
- Significant weight loss

- Bitemporal wasting
- Diffuse loss of subcutaneous adipose tissue
- Hoover sign – paradoxical inward movement of rib cage with inspiration
- Sings of right heart failure – edema, ascites, raised jugular venous pulse

Difference between features of chronic bronchitis and emphysema

	Predominantly Chronic Bronchitis ('Blue-bloater')	Predominantly Emphysema ('Pink-puffer')
Predominant symptom	Cough	Dyspnoea
Sputum	Copious and purulent	Scant and mucoid
Episodes of bronchial infection	More frequent	Less frequent
Episodes of respiratory insufficiency	Frequent	Often terminally
Chest radiograph	Increased bronchovascular markings at lung bases, large heart	Hyperinflation, bullous changes, small and tubular heart
Lung compliance	Normal	Increased
Airways resistance	High	Normal to slight increase
Diffusing capacity	Normal to slight decrease	Decreased
Arterial blood gases	Abnormality early in course of disease	Normal until late
Pulmonary hypertension		
Rest	Moderate to severe	None to mild
Exercise	Worsens	Moderate
Chronic cor pulmonale	Common	Rare except terminally
Cardiac failure	Common	Rare except terminally

Emphysema and chronic bronchitis frequently co-exists because both share common etiology and risk factors.

DIAGNOSIS:

Hallmark of COPD is airflow obstruction, which can be detected by Pulmonary Function testing.

PULMONARY FUNCTION TESTING (SPIROMETRY):

- Spirometry should be performed after the short-acting bronchodilator by inhalational route
- Presence of airflow limitation is confirmed by post-bronchodilator $FEV_1/FVC < 0.70$ [31]
- Severity of COPD can be assessed by FEV_1[34]
- The FEV_1 is often used to assess the clinical course and response to therapy.[32]
- The total lung capacity, functional residual capacity, and residual volume often increase to supernormal values that indicates lung hyperinflation and air trapping.[33]

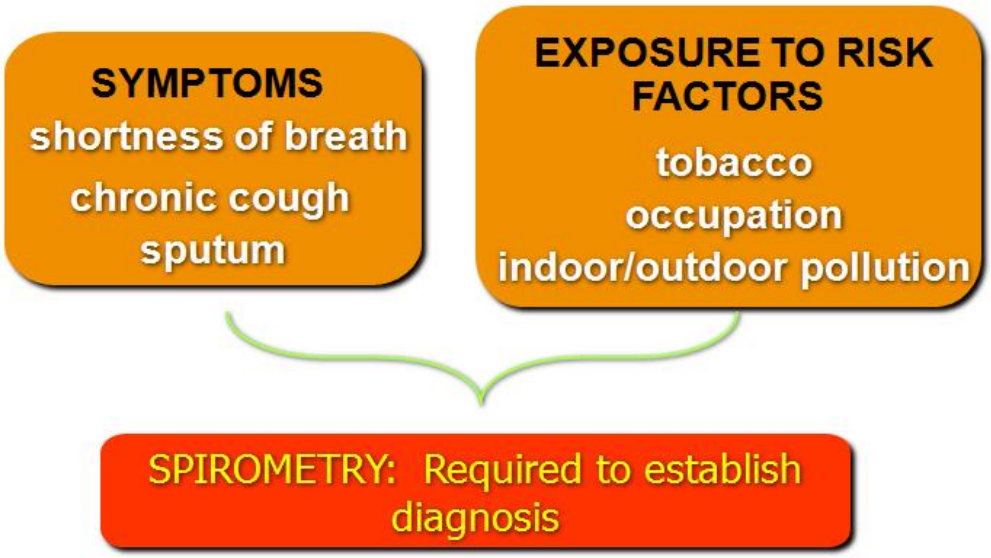
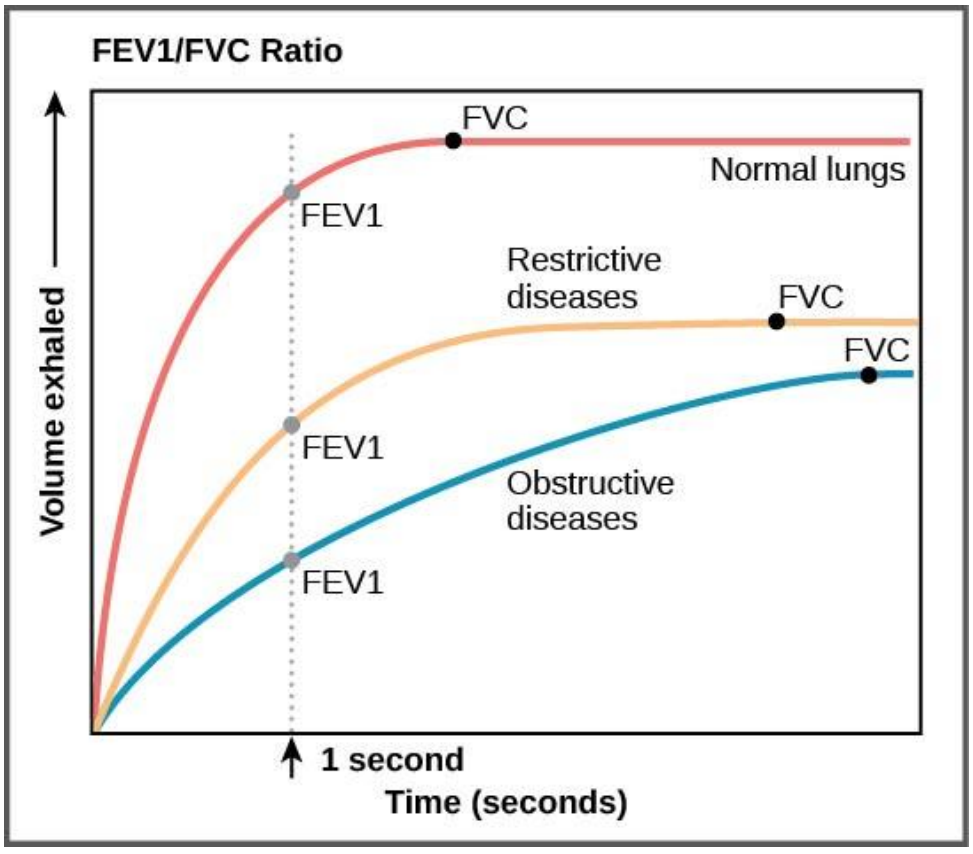


Figure 3. Spirometric evaluation



IMAGING:

- Chest x ray
- HRCT chest

Radiological findings associated with COPD are

- Prominent bronchovascular markings
- Hyperinflated lung fields with diaphragmatic flattening
- Hyperlucency
- Increased retrosternal airspace on the lateral radiograph
- Presence of bullae
- Tubular heart

HRCT chest

- superior to detect the findings of COPD than Chest X ray[37]
- useful for assessment of surgical management[35]

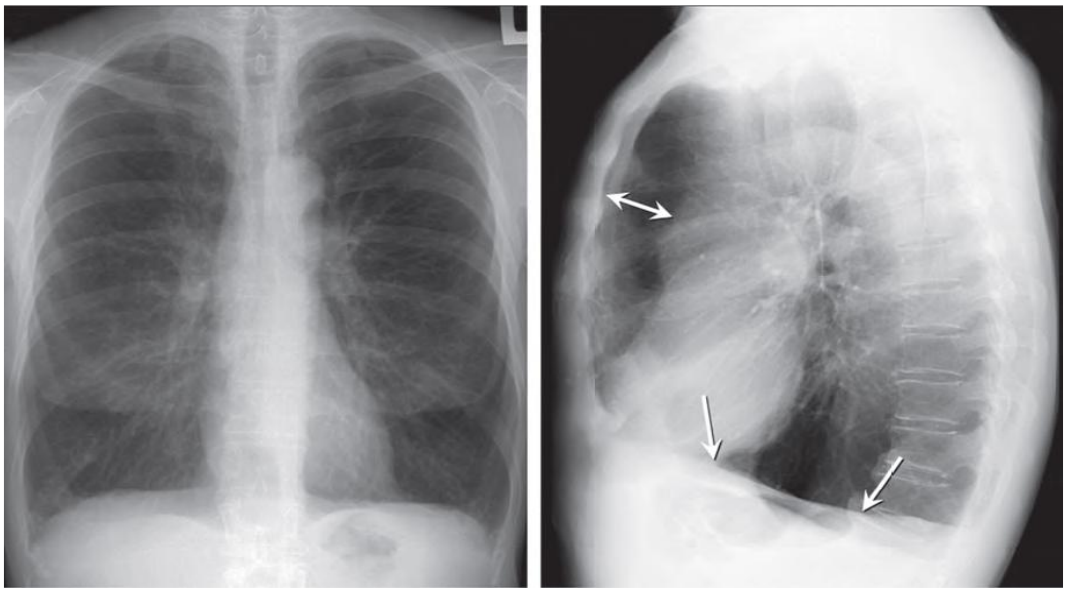


Figure 4a. Picure A: large lung volumes with hyperlucency

Figure 4b. prominent retrosternal clear space of lateral radiograph with flattening of diaphragm

ELECTROCARDIOGRAM:

ECG changes in COPD are[36]

- Right axis deviation
- P-Pulmonale
- RVH pattern
- Right bundle branch block
- Low voltages complexes
- Poor progression of R wave
- Arrhythmias

ECHOCARDIOGRAPHY:

Assessment of cardiac status

pulmonary hypertension

cor pulmonale

RV dysfunction

LV systolic function and ejection fraction

LV diastolic function

PULSE OXIMETRY AND ABG:

Pulse oximetry is usually used to asses O_2 saturation in

Stable patients with FEV_1<35

Signs of respiratory failure

ABG should be assessed when SpO_2 <92%[147] to identify

Hypoxemia (type I respiratory failure)

Hypercapnea (type II respiratory failure)

ALPHA-1 ANTITRYPSIN SCREENING:

Indications for screening

- Young patients (<45 years)

- Lower lobe emphysema
- Family history
- No smoking history

Serum alpha-1antitrypsin levels below 15-20% of normal range is considered as alpha-1antitrypsin deficiency

EXERCISE TESTING:

- 6-minute walk test (6MWT) - frequently employed exercise test
- 6-minute walk distance(6MWD) - The distance that a patient can walk in 6 minutes [40]
- Health status impairment can be assessed by exercise testing and it is one of the prognostic predictor.
- 6MWD is a component of the BODE mortality index[41]
- It can be used to monitor improvement in quality of life, exercise capacity after pulmonary rehabilitation

STAGES OF COPD (GOLD STAGES):

Based on Post bronchodilator FEV_1

GOLD Stage	Severity	Spirometry
I	Mild	FEV_1/FVC <0.7 and FEV_1 ≥80% predicted
II	Moderate	FEV_1/FVC <0.7 and FEV_1 ≥50% but <80% predicted
III	Severe	FEV_1/FVC <0.7 and FEV_1 ≥30% but <50% predicted
IV	Very severe	FEV_1/FVC <0.7 and FEV_1 <30% predicted

Early Stages – Stage I & II

Late Stages – Stage III & IV

BODE INDEX:

Multidimensional grading system which predicts the mortality and survival of the patients with COPD.[41]

Calculation of the BODE Index*				
	Points on the BODE Index			
Variable	0	1	2	3
FEV_1 (% predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 min (meters)	≥350	250–349	150–249	≤149
MMRC dyspnea scale	0–1	2	3	4
Body-mass index (kg/M^2)	> 21	≥21		

Approximate 4 Year Survival Interpretation
0-2 Points: 80%
3-4 Points: 67%
5-6 Points: 57%
7-10 Points: 18%

SEVERITY ASSESSMENT:

By Combined Assessment

- Assess symptoms
- Assess degree of airflow limitation using spirometry
- Assess risk of exacerbations

Assessment of symptoms:

- Modified Medical Research Council questionnaire for breathlessness[43]
- COPD assessment test

Modified Medical Research Council grading for Dyspnoea

Grade	Description of Breathlessness
Grade 0	I only get breathless with strenuous exercise
Grade 1	I get short of breath when hurrying on level ground or walking up a slight hill
Grade 2	On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level
Grade 3	I stop for breath after walking about 100 yards or after a few minutes on level ground
Grade 4	I am too breathless to leave the house or I am breathless when dressing

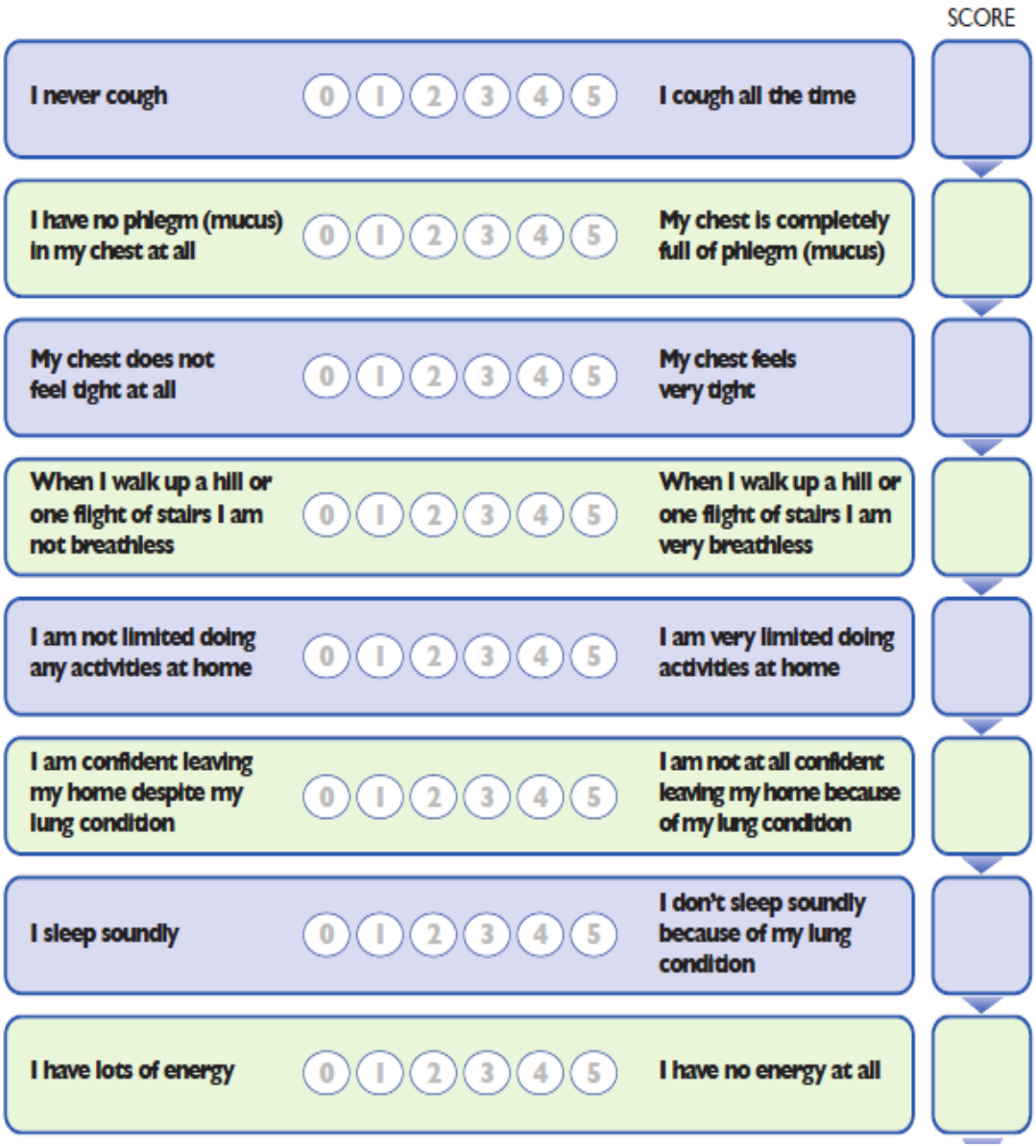
COPD Assessment Test:

Used to asses health status impairment in COPD [42]

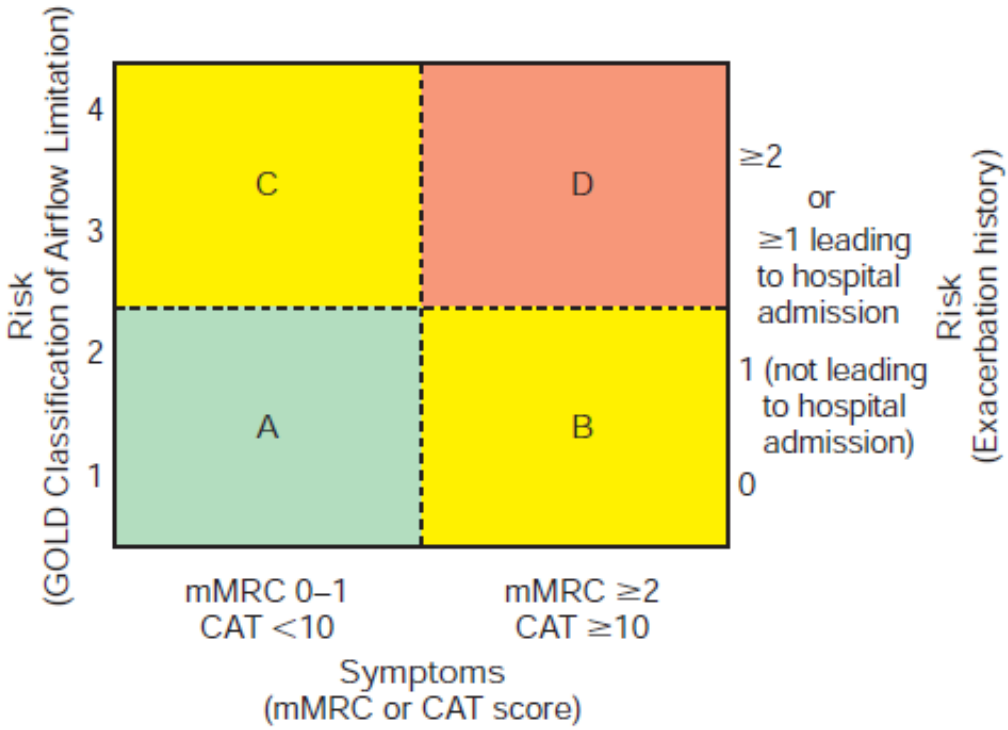
8 measures are used in this test

Score varies from 0-40

CAT test chart



GOLD classification system[44]



Groups of COPD patients (according to GOLD 2015 update)

Group A – Low risk and Less symptoms

- GOLD stage I or II
- No of exacerbation/year 0-1
- No hospitalization
- CAT score <10
- mMRC grade 0-1

Group B – Low risk and More symptoms

- GOLD stage II or II
- mMRC grade 0 $\geq$ 2
- CAT score $\geq$10
- No of exacerbation/year 0-1
- No hospitalization

Group C – High risk and Less symptoms

- GOLD stage III or IV
- mMRC grade 0-1
- CAT score <10
- 2 or more exacerbation/year
- 1 or more hospitalization

Group D – High risk and More symptoms

- GOLD stage III or IV
- 2 or more exacerbation/year
- 1 or more hospitalization
- CAT score $\geq$10
- mMRC grade 0 $\geq$ 2

TREATMENT

Combined approach by

Smoking cessation

Pharmacological therapies

Non pharmacological therapies

Surgical management

SMOKING CESSATION

- most important factor in the management of COPD, since it the main etiological factor
- Smoking cessation slows the progression of reduction in FEV_1[45].
- Multimodality approach including Counseling for smoking cessation and pharmacological therapies is the effective method to treat tobacco addiction
- It is the one of component of Pulmonary rehabilitation
- Improves the survival and outcome of COPD patients
- greater reduction in prevalence of pulmonary complications as well as systemic manifestations

Pharmacological therapy for smoking cessation

Product	Dosing	Side Effects/Precautions
Nicotine Replacement Therapy[a]		
Transdermal patch	7, 14, or 21 mg/24 hr Usual regimen = 21 mg/d × 6 wk, 14 mg/d × 2 wk, 7 mg/d × 2 wk[b]	(Apply to all nicotine products) Headache, insomnia, nightmares, nausea, dizziness, blurred vision
Chewing gum, lozenges	2–4 mg q1–8h Gradually taper use	
Inhaler	10 mg/cartridge (4 mg delivered dose) 6–16 cartridges/d	
Nasal spray	0.5 mg/spray 1–2 sprays in each nostril q1h	
Nonnicotine Pharmacotherapy		
Bupropion ER (*Zyban*)	150 mg/d × 3 d, then bid × 7–12 wks Start 1 wk before quit date	Dizziness, headache, insomnia, nausea, xerostomia, hypertension, seizure Avoid monoamine oxidase inhibitors
Varenicline (*Chantix*)	0.5 mg/d × 3 d, bid × 4 d, then 1 mg bid × 12–24 wk Start 1 wk before quit date	Nausea, vomiting, headache, insomnia, abnormal dreams Worsening of underlying psychiatric illness

PHARMACOLOGICAL THERAPIES

Bronchodilators

- Beta 2 agonists
- Methylxanthines
- Anticholinergics

Inhaled corticosteroids

PDE-4 inhibitors

Mucolytic and antioxidant agents

Anti tussives

Patient Group	Recommended First choice	Alternative Choice	Other Possible Treatments[†]
A	SAMA prn *or* SABA prn	LAMA *or* LABA *or* SABA and SAMA	Theophylline
B	LAMA *or* LABA	LAMA and LABA	SABA *and/or* SAMA Theophylline
C	ICS + LABA *or* LAMA	LAMA and LABA *or* LAMA and PDE4-inh. *or* LABA and PDE4-inh.	SABA *and/or* SAMA Theophylline
D	ICS + LABA *and/or* LAMA	ICS and LABA and LAMA *or* ICS and LABA and PDE4-inh. *or* LAMA and LABA *or* LAMA and PDE4-inh.	Carbocysteine *SABA and/or* SAMA Theophylline

SABA – Short acting beta2 agonists

LABA – Long acting Beta 2 agonists

SAMA – Short acting antimuscarinic agents

LAMA – Long acting antimuscarinic agents

ICS – Inhalational Corticosteroids

PDE- 4 inh – Phosphodiesterase 4 Inhibitors

Bronchodilators

Increase FEV_1 by altering airway smooth muscle tone

Reduce dynamic hyperinflation during exercise was well as rest[48]

Improve exercise performance[47]

Inhaled therapies are preferred

Long acting inhaled bronchodilators are more effective and more symptom relief and also more convenient

$Beta_2$ agonists

Short acting

Salbutamol, Levalbuterol, Fenoterol, Terbutaline

Long acting

Salmeterol, Formoterol, Arformoterol, Tulobuterol, Indacaterol

Side effects – tremor, tachycardia, hypokalemia

Anticholinergics

Short acting - Ipratropium bromide, oxitropium bromide

Long acting – glycopyrronium bromide, tiotropium, aclidinium bromide, umeclidinium

Side effects – dryness of mouth

Methylxanthines

Aminophylline, theophylline

Theophylline – most commonly used

Less effective and less tolerated than long acting inhaled bronchodilators

Low dose theophylline reduces exacerbations usually but there is post-bronchodilator improvement in lung function

Use of combination with different pharmacological classes of bronchodilators usually improve efficacy of therapy and also decreased side effect profile. It is better than increasing the dose of a single bronchodilator.[49]

Inhaled corticosteroids

Drugs – budesonide, beclomethasone, fluticasone

- Regular treatment with ICS therapy in COPD patients with an FEV_1 < 60%, improves the lung function and respiratory symptoms, and also improves the quality of life and reduces frequency and duration of exacerbations.[51]
- Inhaled steroids treatment withdrawal may lead to acute exacerbations in some patients

- There is increased risk of lung infection like pneumonia associated with inhalational steroid therapy
- Adverse effects – hoarse voice, oral candidiasis, skin bruising
- An ICS combined with a LABA is more effective in
    - reducing acute exacerbations in severe COPD patients[52]
    - improving health status and lung function

Oral corticosteroids

Chronic treatment with systemic corticosteroids should be avoided because of an unfavorable benefit-to-risk ratio

Roflumilast

- inhibitor of phosphodiesterase-4 enzyme
- It inhibits the break down of intracellular cAMP and there by it reduces inflammation
- Dose once a day schedule (500 mg)
- Roflumilast along with long-acting β2 agonists reduce exacerbations in COPD[53]
- Adverse effects - nausea, diarrhoea, sleep disturbances, headache, and weight

Vaccines:

Recommended vaccination in COPD are

- Influenza vaccine [54]
- Pneumococcal polysaccharide vaccine[55]

Effects of Vaccination in COPD patients

- reduce respiratory tract infections that leads to prevention of acute exacerbations which requires hospitalization and there is definite morbidity and mortality benefits
- decrease the prevalence of community acquired pneumonia

Oxygen therapy:

Long-term oxygen therapy increase survival of COPD patients with respiratory failure. LTOT means oxygen therapy with more than 15 hours/day.

Indications for LTOT:

- SaO2 less than 88% (or) PaO2 less than 55 mm Hg with or without hypercapnia for two times in a three week period.
- PaO2 between 55 mm Hg and 60 mm Hg with presence of Pulmonary arterial hypertension, Congestive cardiac Failure and Secondary Polycythemia (Hct >55).[56]

PULMONARY REHABILITATION:

One of the main component in the managment of COPD.

The pulmonary rehabilitation programme includes

- Exercise Training
- Smoking Cessation
- Nutrition Counseling
- Education

The major benefits of the rehabilitation programme are:

Results of Pulmonary Rehabilitation
Decreases in Medical resource utilization (e.g., hospitalizations, emergency room visits) Respiratory symptoms (e.g., breathlessness) Psychological symptoms (e.g., depression, fear)
Increases in Quality of life Physical activity Exercise tolerance (endurance or maximal level of activities of daily living) Knowledge Independence
Return to work possible
No change in lung function
Possible prolonged survival

Pulmonary rehabilitation programme with exercise training of at least four weeks has been shown that there is significant improvement in health related quality of life and mortality.[57]

Nutritional support:

- BMI is one of the independent prognostic and mortality predictor in COPD patients.
- Low Body mass index and nutritional depletion are the factors associated with poor prognosis.
- Ghrelin, Growth hormone releasing peptide, decreases the utilization of peripheral fat and stimulates good appetite by GH-independent mechanisms, which lead to positive energy balance
- Ghrelin level was decreased in COPD
- Nutritional supplementation should be a part of integrated rehabilitation programme with exercise training, because nutritional support have significant role in the management of COPD.[60]

PATIENT EDUCATION:

Patient Education Topics for Office Management of COPD
Risk factors for COPD
Smoking cessation advice and instruction
Reduction of noxious environmental exposures
Immunization for influenza and pneumococcus
Nature and prognosis of COPD
Indications, dose, benefits, and adverse effects of medications
Proper inhaler and nebulizer use
Strategies to improve adherence with prescribed treatment
Pacing, arm support, and other strategies to minimize dyspnea
Importance of regular exercise and social interaction
Options for pulmonary rehabilitation programs
Recognition and early treatment of exacerbations
Indications for and proper use of supplemental oxygen
Options for surgical management if indicated
Advanced directives for end-of-life care

SURGICAL MANAGEMENT

Lung volume reduction surgery (LVRS):

LVRS not only increase exercise capacity but also improve the Quality of Life in COPD patients, most benefit in patients with upper lobe emphysema and with poor exercise capacity.

It should not be performed in patients with non-upper lobe emphysema and with high baseline exercise capacity, since mortality is increased in these patients. So they are poor candidates for LVRS[58]

Lung transplantation:

Transplantation of lung is another option in patients with FEV_1 < 25% and/or paCO2 > or = 55 mm Hg.

Survival rates after lung transplantation approximately

80% at one year

50% at five years

35% at ten years

Bronchiolitis obliterans - long-term complication of lung transplantation which can result in decline of lung function.[59]

PULMONARY COMPLICATIONS OF COPD

- Recurrent episodes of acute exacerbation by viruses and bacteria
- Pneumothorax
- Chronic and Acute on Chronic respiratory failure
- Pulmonary artery hypertension
- Cor pulmonale
- Right heart failure

ACUTE EXACERBATIONS:

Definition:

Acute exacerbation is defined as "acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day to-day variations and leads to a change in medication" [61]

Triggers:

- Viral or bacterial infections – most common[62]
- Air pollutants [63]
- 30% - no cause

Frequent exacerbations is defined as "two or more exacerbations per year"[64]

Management is challenging one for frequent exacerbators.

Cardinal features of exacerbations

Increase in dyspnoea, sputum volume, sputum purulence

Common pathogens involved in acute exacerbation are

- Streptococcus pneumoniae
- Haemophilus influenzae
- Pseudomonas aerugenosa
- Moraxella catarrhalis

Differential diagnosis of COPD exacerbations

- Congestive cardiac failure
- Pneumothorax
- Pneumonia
- Pulmonary embolism
- Cardiac arrhythmias
- Pleural effusion

Treatment of exacerbations

- Bronchodilators
- Corticosteroids
- Antibiotics

- Inhalational short-acting bronchodilators with β2-agonists and anticholinergics should be preferred in exacerbation[65] and given either by nebulizers or by metered-dose inhalers.

- Methylxanthines (theophylline or aminophylline i.v.) can be used if inadequate response to inhaled short-acting bronchodilators[66].

- Systemic corticosteroids

  reduce risk of treatment failure, early relapse

  shortens recovery time and hypoxemia[67]

  decrease length of hospital stay

  Oral prednisolone 30-40 mg daily for 10-14 days

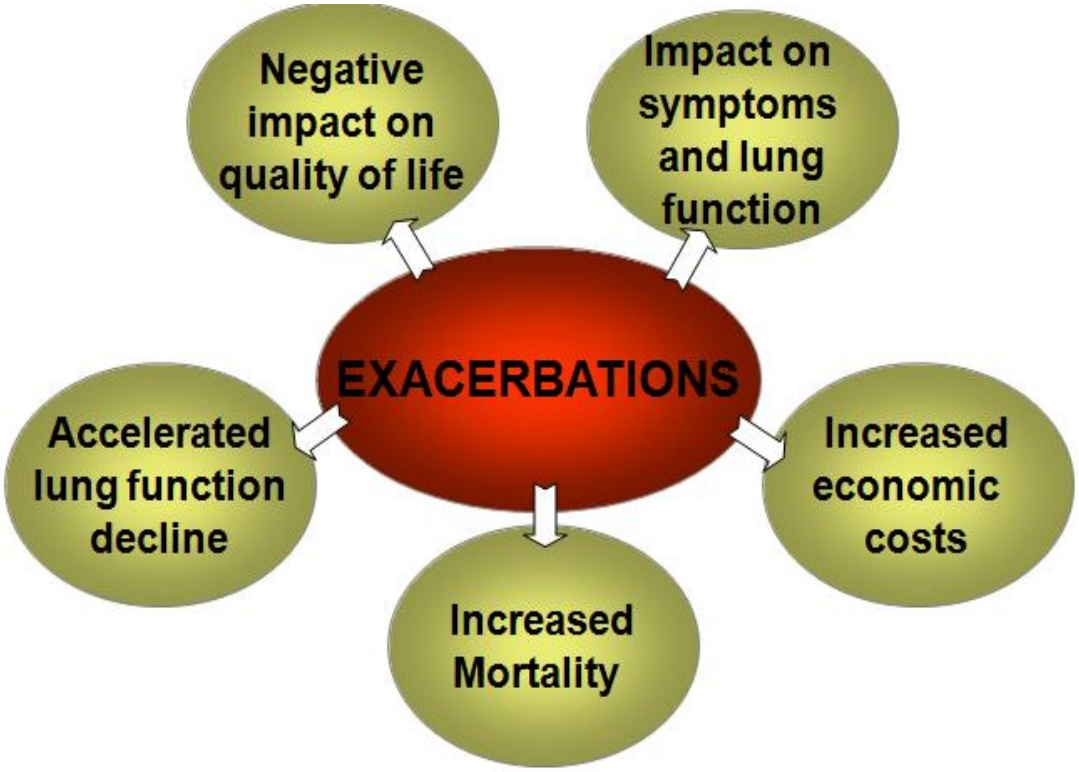
  Nebulized budesonide is an alternative

- Supplemental O_2 therapy to maintain SaO_2 88 to 92%.

- Mechanical ventilation if needed

Prevention of exacerbation

- Smoking cessation
- Influenza and pneumococcal vaccination
- Pulmonary rehabilitation
- Knowledge about current therapy and inhaler technique
- Treatment with long acting inhaled bronchodilators



Effects of exacerbations in the course of disease

PULMONARY HYPERTENSION

Usually develop in the late course of COPD.

Mechanisms are

- hypoxic vasoconstriction of small pulmonary arteries
- endothelial dysfunction results from Inflammation
- loss pulmonary capillary bed in emphysema increases pressure in pulmonary circulation

Pulmonary hypertension can progress to Cor Pulmonale and Right Heart Failure

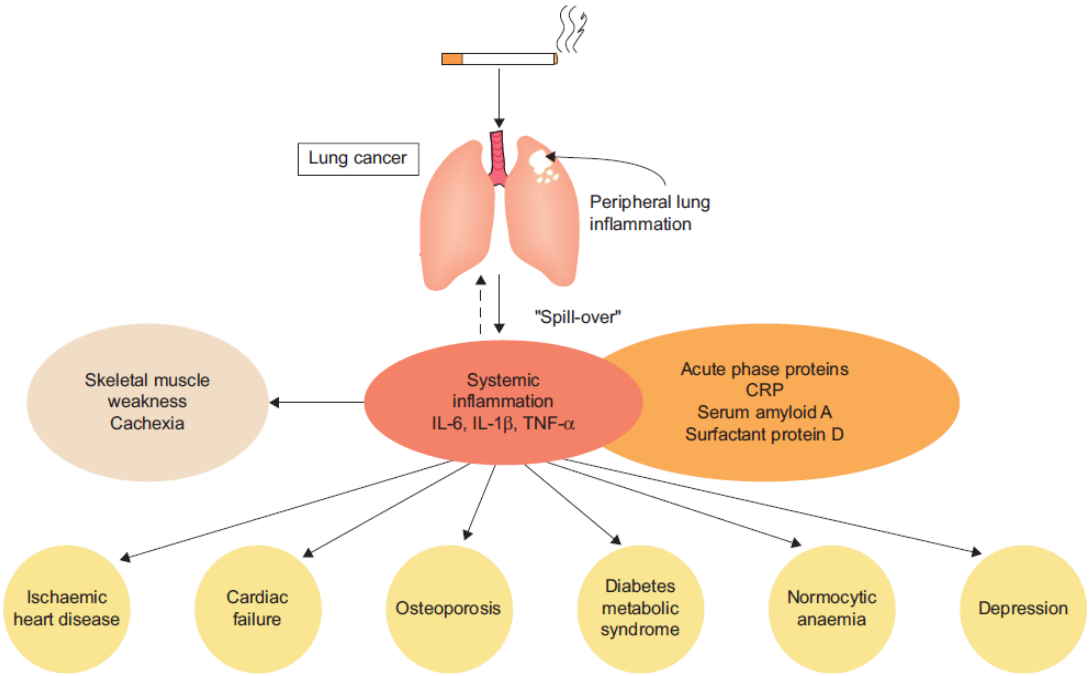
SYSTEMIC MANIFESTATIONS OF COPD:

Patients with COPD may have variety of comorbid illness due to its systemic nature of disease. Following systemic manifestations are reported with COPD

- Cachexia: loss of fat-free mass
- Skeletal muscle wasting
- Pulmonary hypertension

- Congestive cardiac failure
- Lung cancer (small cell, nonsmall cell)
- Ischemic heart disease
- Osteoporosis
- Normocytic anaemia
- Obstructive sleep apnoea
- Diabetes
- Metabolic syndrome
- Depression

Figure 5. Pathogenesis of systemic manifestations of COPD



Mechanism of systemic manifestation:

There are two theories for explaining systemic manifestations

1. Spillover of inflammation from the lung into the systemic compartment

2. Pro-inflammatory phenotype – systemic inflammation occurs independent of pulmonary inflammation. [68]

Pathological mechanisms of the Systemic Inflammation

1. Smoking causes systemic inflammation by promoting vascular endothelial dysfunction and by generating oxidative stress. These changes also occur even in passive smokers and smokers of only a few pack-years.[69]

2. Hypoxia leads to generation of Hypoxia inducible factor-1. This factor activates numerous genes involved in erythropoiesis, energy metabolism, angiogenesis, vascular remodelling, inflammation and cell proliferation[70]. Hypoxemia results in elevation of TNF-α level, and its elevated levels were associated with the severity of hypoxemia. Domiciliary oxygen therapy (LTOT) improves

survival of patients, since it decreases systemic inflammation by reducing the hypoxemia and related changes.

3. Adipokines were also demonstrated in COPD patients and its association with development of comorbidities. Circulating leptin, one of the factor which promote systemic inflammation in stable COPD patients. Increased leptin levels may lead to decline in pulmonary function in smokers with COPD, independent of obesity [71]

4. COPD induces the development of anti-elastin antibodies, which is responsible for auto immunity that explain the progression of COPD even after stopping of smoking.[72]

5. Accelerated lung ageing occurs in COPD may also responsible the systemic inflammation and development of co morbidities. COPD is a state of oxidative stress which can cause telomere shortening that results in increased ageing process in the lung and other systems.[73]

CARDIOVASCULAR MANIFESTATIONS OF COPD:

- Coronary artery disease
- Left ventricular diastolic dysfunction
- Congestive heart failure
- Atrial fibrillation
- Ventricular arrhythmias

Poor lung function is the main risk factor for LV diastolic dysfunction, atrial fibrillation, and ventricular dysarrhythmias

Coronary artery disease:

- COPD and CAD are closely related, there is 3-fold cardiovascular risk in COPD while compared to other population
- Concomitant involvement of COPD and CAD increase the morbidity and mortality
- Systemic inflammation in COPD is the important pathogenesis for development of atherosclerosis and ischemic heart disease.[74]
- Airflow limitation significantly increases the risk myocardial infarction and its related death in patients with COPD. This can be occur irrespective of age, sex and smoking history[75]

- Ischemic heart disease in COPD patients can be managed according to IHD guidelines in the presence of COPD. Treatment with Cardioselective Beta blockers is considered safe.

Heart failure:

- It is another common co morbidity in patients with COPD.
- 30% of stable COPD patients have some degree of Heart failure
- Acute heart failure and acute exacerbation of COPD often coexists, that increases the morbidity and mortality
- Heart failure in COPD can be managed according to usual HF guidelines. Selective beta1 blockers significantly improves the survival[76]. Bisoprolol is superior to carvedilol on respiratory parameter.

Atrial fibrillation:

- AF is the most common arrhythmia encountered in COPD
- Increases the breathlessness and disability, when coexists with COPD.
- Treatment according to usual AF guidelines
- Cardioselective beta blockers are preferred, when beta blockers are used.

LV DIASTOLIC DYSFUNCTION AND COPD:

There many mechanisms that explain the presence of left ventricular diastolic dysfunction in COPD

- Chronic hypoxemia results in intracellular calcium transport disturbances that leads to abnormalities of myocardial relaxation[77,78]

- Presence of cor pulmonale (secondary to pulmonary hypertension) results in interventricular septum deviation toward left ventricle. These changes may lead to alteration in left ventricular geometry and impairs the ventricular filling.[80]

- Presence of emphysema and hyperinflation impairs left ventricle filling.[81] Cardiac function may be impaired as a result of raised intrathoracic pressures which may lead to decrease in preload and increase in left ventricular afterload.[82]

- Airflow limitation and Systemic Inflammation which are responsible for atherosclerotic plaque formation that can lead to myocardial ischemia and left ventricular diastolic dysfunction.[83]

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION:

LV diastolic function can be asses by Doppler echocardiography

By assessing mitral inflow signal

E wave – early diastolic LV filling

A wave – late diastolic LV filling due to atrial contration

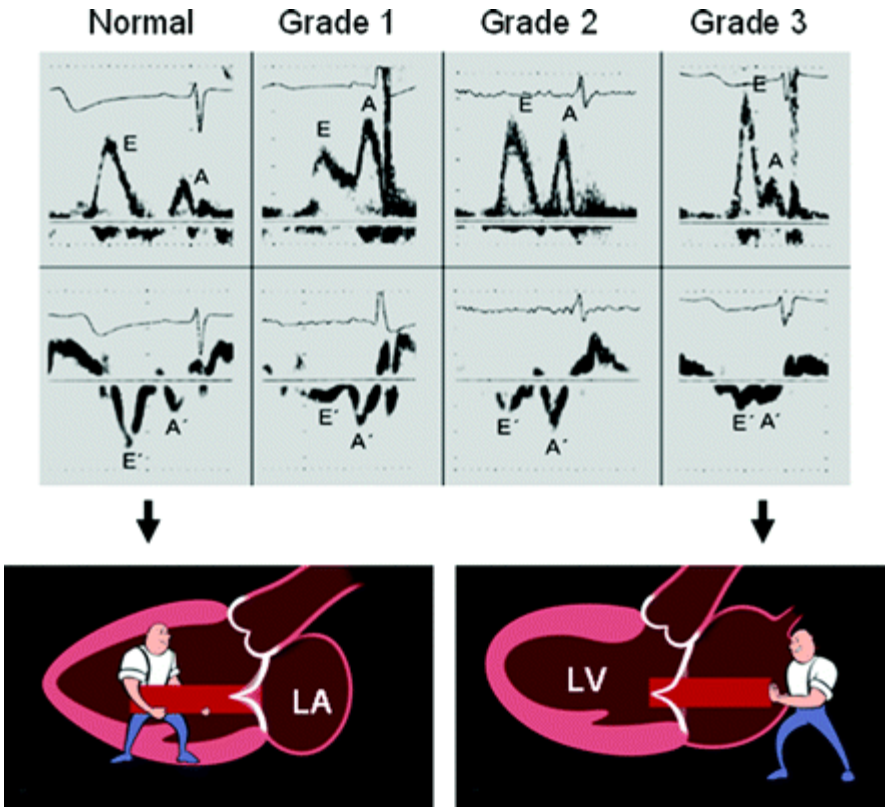
DT – deceleration time of E wave

IVRT - Isovolumetric relaxation time

Grading of LV diastolic dysfunction:

Grade I	Impaired relaxation
Grade II	Pseudo normal filling pattern
Grade III	Reversible restrictive filling pattern
Grade IV	Irreversible restrictive filling pattern

Figure 6. Grades of LV diastolic dysfunction



Normal diastolic function

E-wave is taller than the A-wave.

The E/A ratio will be between 1 and 2.

The shape of the E-wave is quite symmetrical and the normal deceleration time is between 150 ms and 200 ms.

IVRT is 50 - 100 ms.

Impaired relaxation - grade I diastolic dysfunction:

- Magnitude of the E-wave decreases (stiff ventricle impairs early ventricle filling)
- IVRT increases (> 100 ms)
- A-wave will be larger (due to effective atrial contraction)
- E-wave (E/A ratio < 1)
- DT will also be prolonged (≥ 240 ms).

Pseudo normal filling pattern - grade II diastolic dysfunction:

- Ongoing diastolic dysfunction may lead rise in LA pressure
- Pressure gradient between LA and LV increases, so there is increased force to fill the ventricle during early diastole. This lead to increase in size of the E-wave compared to A wave
- E/A ratio become to 0.8 - 1.5.
- DT and IVRT (< 90 ms) also decrease
- This looks similar to "normal" diastolic function and so referred as "pseudonormal"
- Valsalva maneuver unmask elevated filling pressures by decreasing the preload. So there is reversal of the pattern to grade I LVDD during the maneuver.

Reversible restrictive filling pattern - grade III diastolic dysfunction:

- Progressive and further rise in filling pressure leads to further increase the pressure gradient between LA and LV.
- E-wave become more tall, and the A-wave become short.
- The E/A ratio ≥ 2
- Short DT (<160 ms) and IVRT ($\leq$ 80 ms). LV filling starts early and also terminate quickly due to elevated filling pressure
- Valsalva maneuver reverses the restrictive filling to a "pseudonormal" pattern (grade II).

Irreversible restrictive filling Pattern - grade IV diastolic dysfunction:

- It is the most severe form of dysfunction
- Valsalva maneuver is unable to reverse the pattern to a pseudonormal one. This is the differentiating feature between grade III and IV
- These patients are usually symptomatic and have advanced forms of heart failure.

EFFECTS OF LV DIASTOLIC DYSFUNCTION IN COPD:

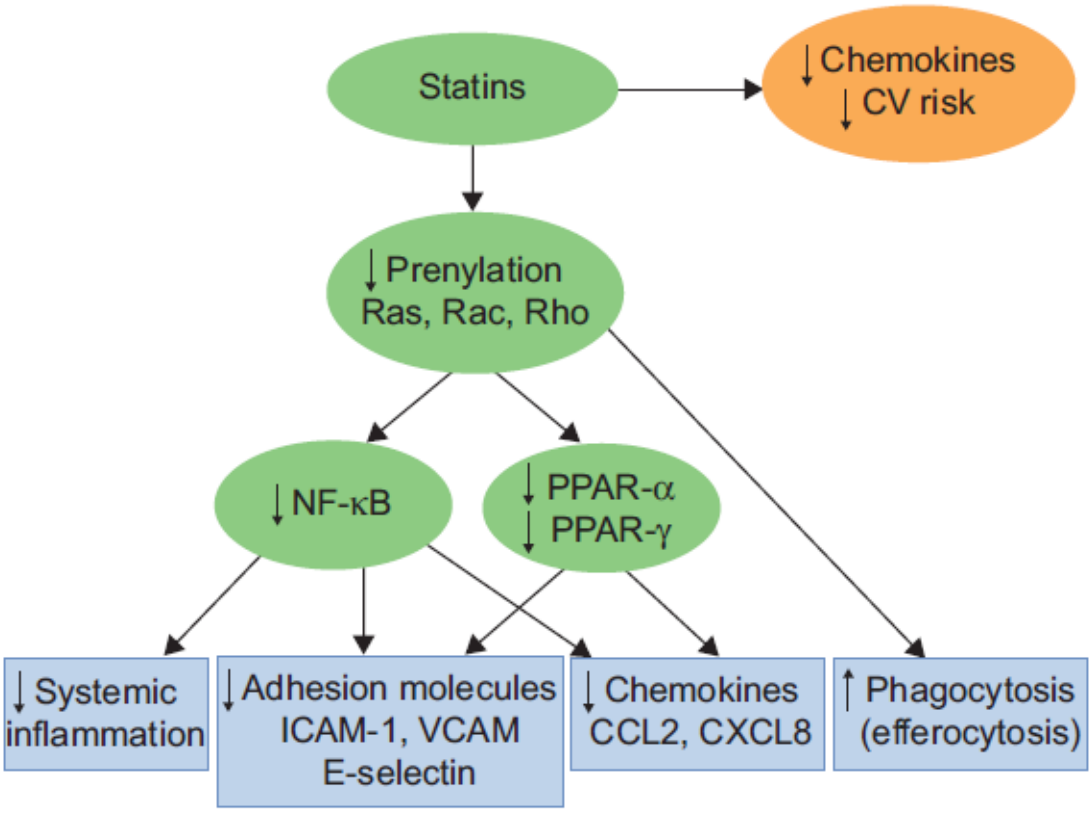
- LV diastolic dysfunction may be asymptomatic or it can present with classical heart failure symptoms - diastolic heart failure.
- more common in older women
- prevelance increases with age[83]
- Its prevalence also increases with stages of COPD. More common in later stages of COPD[84]
- Other risk factors for developing diastolic heart failure are[88]
    - Hypertension
    - Diabetes mellitus
    - Obesity
    - Ischemic heart disease
- Diastolic heart failure increases the mortality and morbidity when coexists with COPD
- Left ventricular diastolic dysfunction increases risk of exacerbation and prolongs the hospitalization [87]
- Mortality rates of COPD with left ventricular diastolic dysfunction
        - 29% at one year
        - 65% after five years [86]

- It is very essential to exclude heart failure during acute exacerbation of COPD.[85]

DRUGS ASSOCIATED WITH IMPROVED CARDIOVASCULAR OUTCOME

- Statins
- ACE inhibitors
- Beta blockers

Role of statins:



Statins not only reduce cholesterol but also exert several other pharmacological actions including [89]

- anti-inflammatory
- antioxidant
- immunomodulation

Statins have favourable effects on cardiovascular disease and improves the outcome of COPD patients associated with co morbidities.[90]

ACE inhibitors:

- ACEIs are used to treat heart Failure and hypertension in COPD.
- ACE inhibitors have been shown that to reduce pulmonary hypertension.
- It may reduce exacerbations and has mortality benefits in patients with COPD.[91]
- May reduce pro-inflammatory effects of angiotensin.[92]

Beta blockers:

Long-term cardioselective beta-blocker are safe and well-tolerable in patients with COPD.

Beta-blocker co-prescription in COPD have favourable cardio-vascular outcome and improves the survival.[76]

MATERIALS AND METHODS

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SOURCE OF DATA:

Patients admitted in Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3, diagnosed to have Chronic Obstructive Pulmonary Disease, fulfilling the inclusion and exclusion criteria were included in the study group. 100 such patients were taken up for this study.

STUDY DESIGN:

A hospital based observational study

STUDY DURATION:

6 months: March 2015-August 2015

INCLUSION CRITERIA:

Proven cases of chronic obstructive pulmonary disease by clinical, imaging, and Pulmonary Function Test.

EXCLUSION CRITERIA:

- Patients with co morbid illness Diabetes Mellitus, Hypertension, Chronic Kidney Disease
- Coexisting intrinsic heart disease like coronary artery disease, valvular heart diseases
- Patients with coexisting with other lung pathologies

DATA COLLECTION AND METHODS:

Data was collected in a pretested proforma from eligible patients. 100 patients were selected on the basis of simple random sampling. They were subjected to detailed history taking and clinical examination. The following investigations were done.

- Chest X-ray
- Electrocardiogram
- Pulmonary function test
- Echocardiogram

PFT – Pulmonary function test:

All patients were subjected to PFT using spirometer in the standing position according to standard procedures. Following measurements were obtained

- Forced expiratory volume in one second (FEV1),
- Forced vital capacity (FVC),

Predicted values for each of the parameters were obtained from standardized references.

ECHOCARDIOGRAPHY:

A 2-D transthoracic echocardiography was done for all patients to asses chambers size, systolic and diastolic functions of LV, presence of Pulmonary hypertension and RV function. LV diastolic function was assessed and graded by Doppler echocardiography by assessing mitral inflow signal, E/A ratio, deceleration time of E wave (DT), Isovolumetric relaxation time (IVRT).

STASTICAL METHODS APPLIED:

Datas were analysed using the SPSS software. Statistical significance was indicated by the Chisquare test. Variables were considered to be significant if $p<0.05$.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

Table1. AGE DISTRIBUTION

Age group (years)	Frequency	Percent
<40	2	2.0
41-50	20	20.0
51-60	39	39.0
> 60	39	39.0
Total	100	100.0

Most cases of COPD occur in the age group 51-60 years and above 60 years 78% of cases are above 50 years

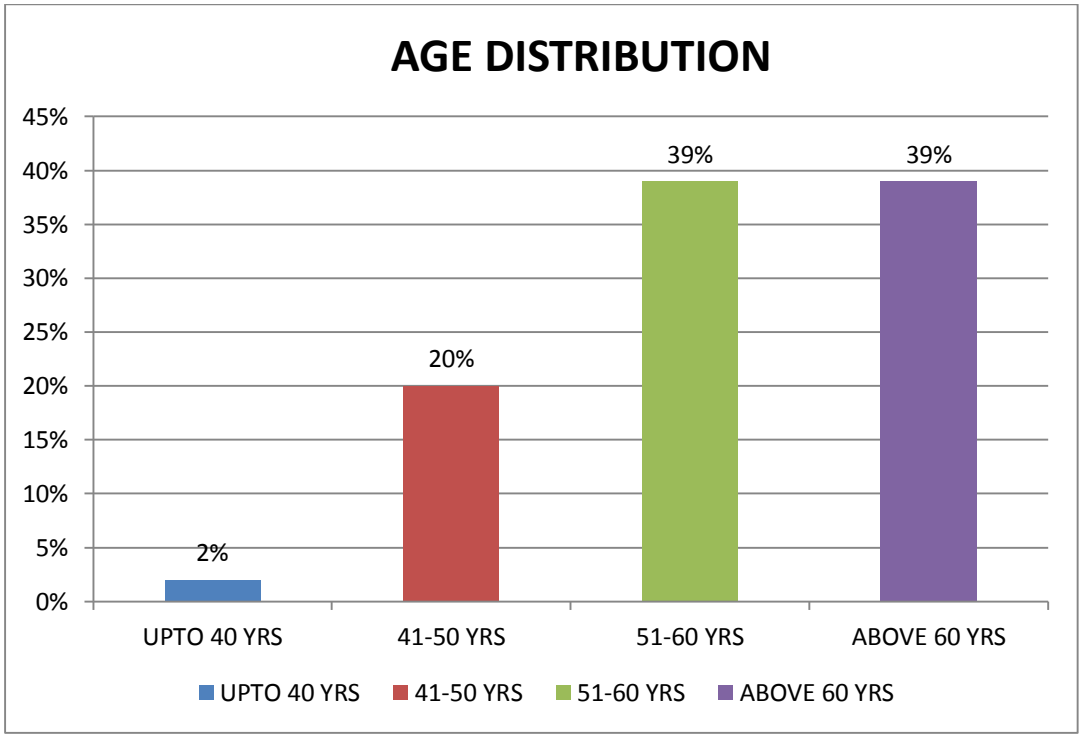
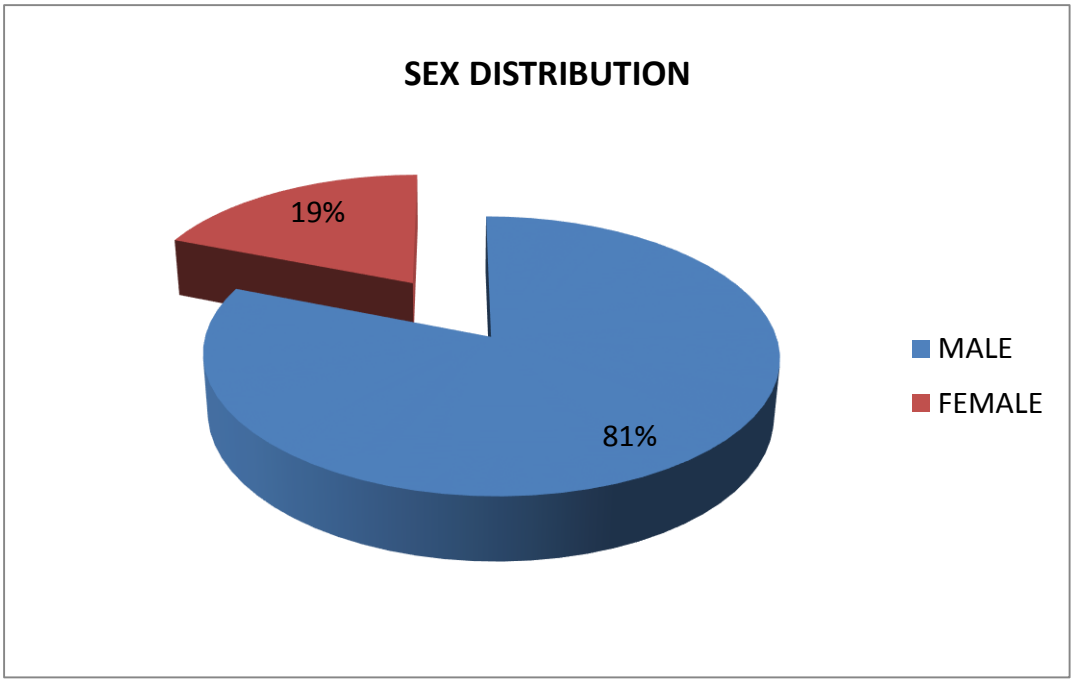


Table 2. SEX DISTRIBUTION

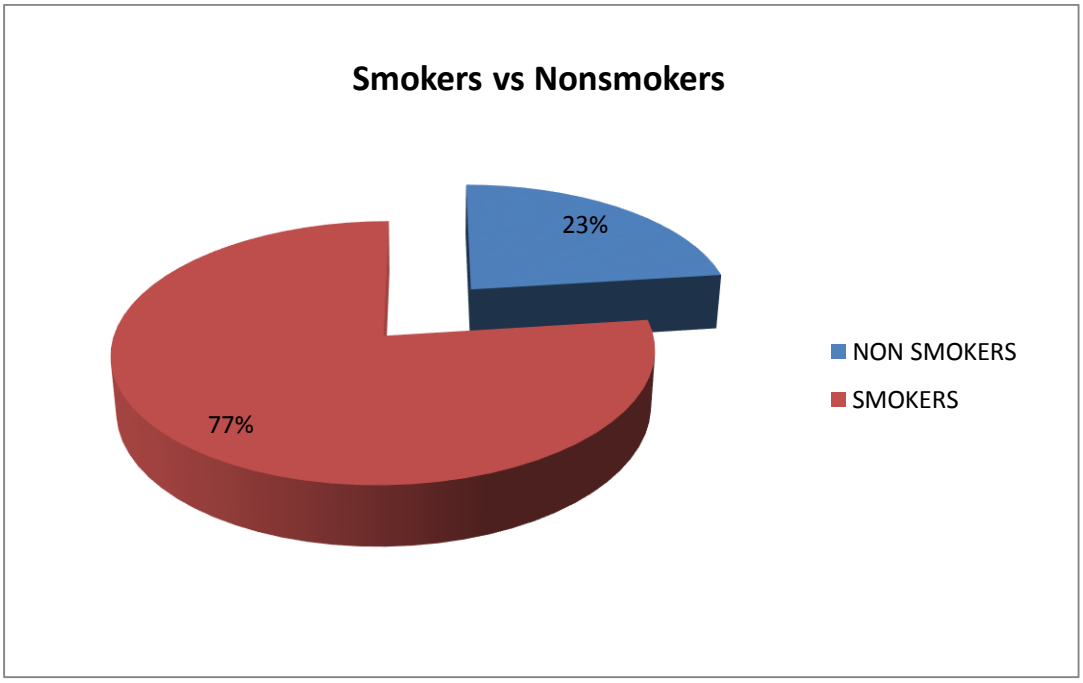
Sex	Frequency	Percent
MALE	81	81.0
FEMALE	19	19.0
Total	100	100.0



Among 100 patients 81% were male, 19% were female

Table 3. Smokers vs Nonsmokers

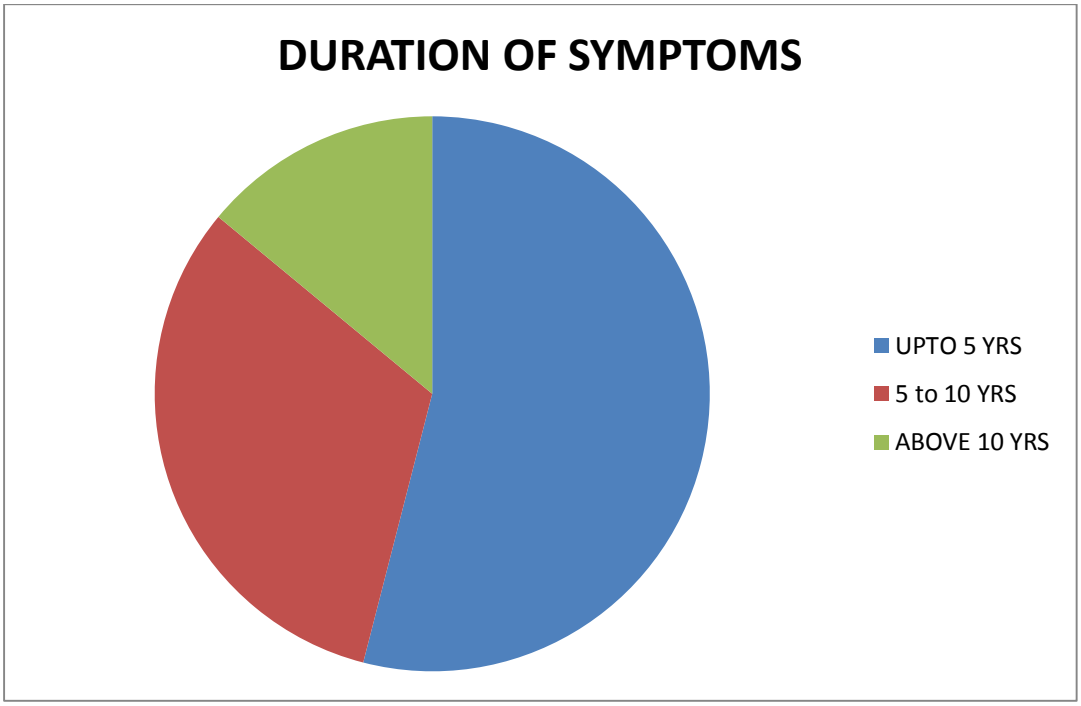
	Frequency	Percent
NON SMOKERS	23	23.0
SMOKERS	77	77.0
Total	100	100.0



In our study, majority of COPD patients in our study are smokers (77%).

Table 4. DURATION OF SYMPTOMS

Duration of symptoms (years)	Frequency	Percent
< 5	54	54.0
5-10	32	32.0
>10	14	14.0
Total	100	100.0



In our study, majority of patients had duration of symptoms <5 years (54%). Patients with symptoms more than 10 years are least common.

Table 5. Stages of COPD (GOLD Stages)

Stages	Frequency	Percent
I	16	16.0
II	40	40.0
III	30	30.0
IV	14	14.0
Total	100	100.0

In our study among 100 patients, 16 patients were in stage I, 40 were in Stage II, 30 were in Stage III, 14 were in Stage IV. Most patients were in stage II and III (70%). Early stages (I &II) – 46%, Late stages (III&IV) – 54%.

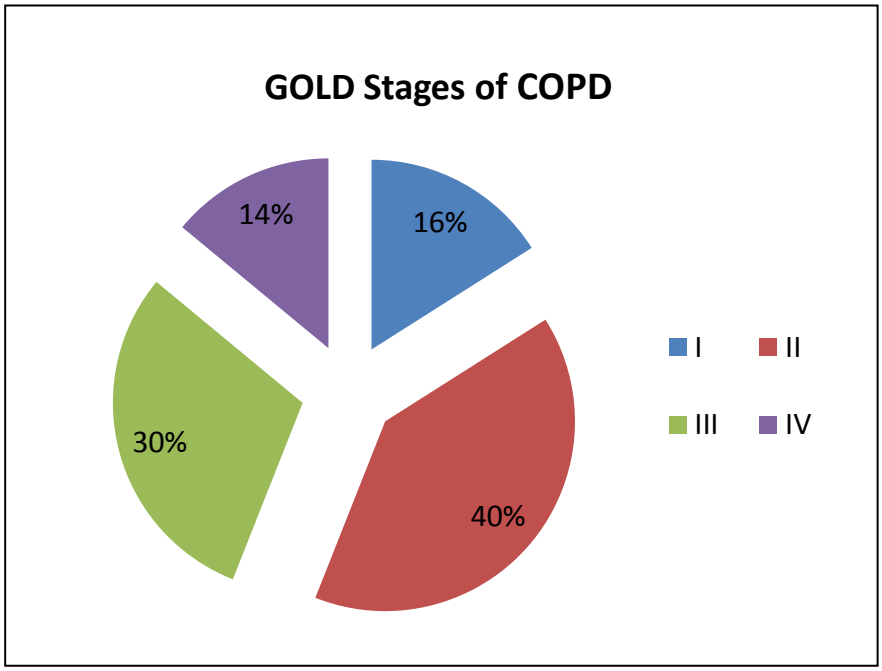
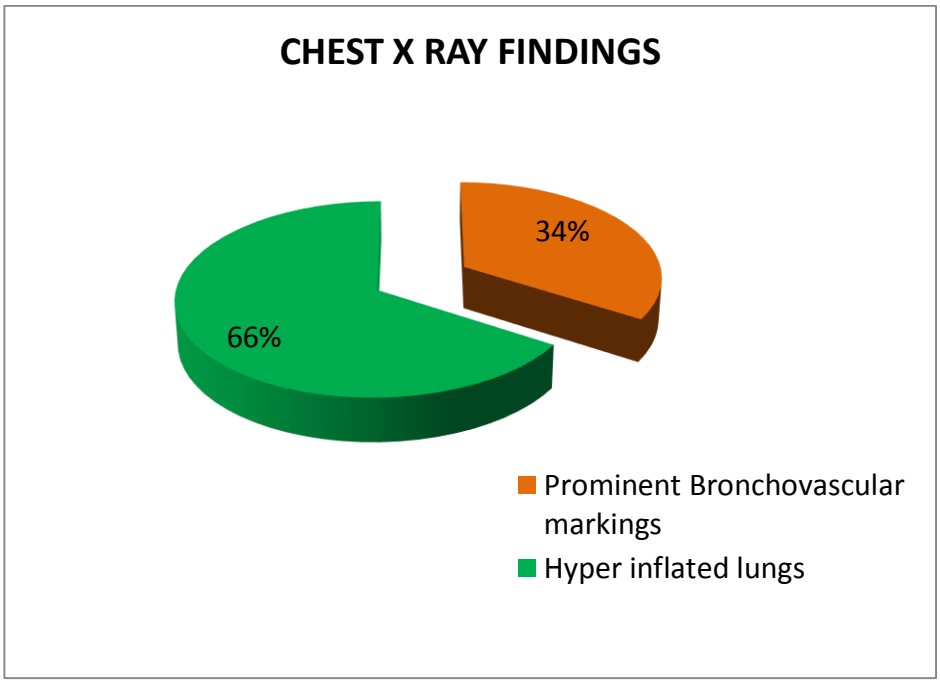


Table 6. Chest x ray findings

CXR Findings	Frequency	Percent
Prominent Bronchovascular markings	34	34.0
Hyperinflated Lungs	66	66.0
Total	100	100.0



In our study, hyperinflated lung field is the common chest x ray findings. 66% of patients had hyperinflated lungs. 44% had finding of Prominent Bronchovascular markings.

Table 7. ECG FINDINGS

ECG findings	Frequency	Percent
P – Pulmonale	30	30.0%
RVH	10	10.0%
RAD	32	32.0%
RBBB	12	12.0%
PPRW	26	26.0%
Low voltage complexes	18	18.0%

Most common ECG finding in our study population is Right Axis Deviation (32%). P-Pulmonale found in 30% of patients.

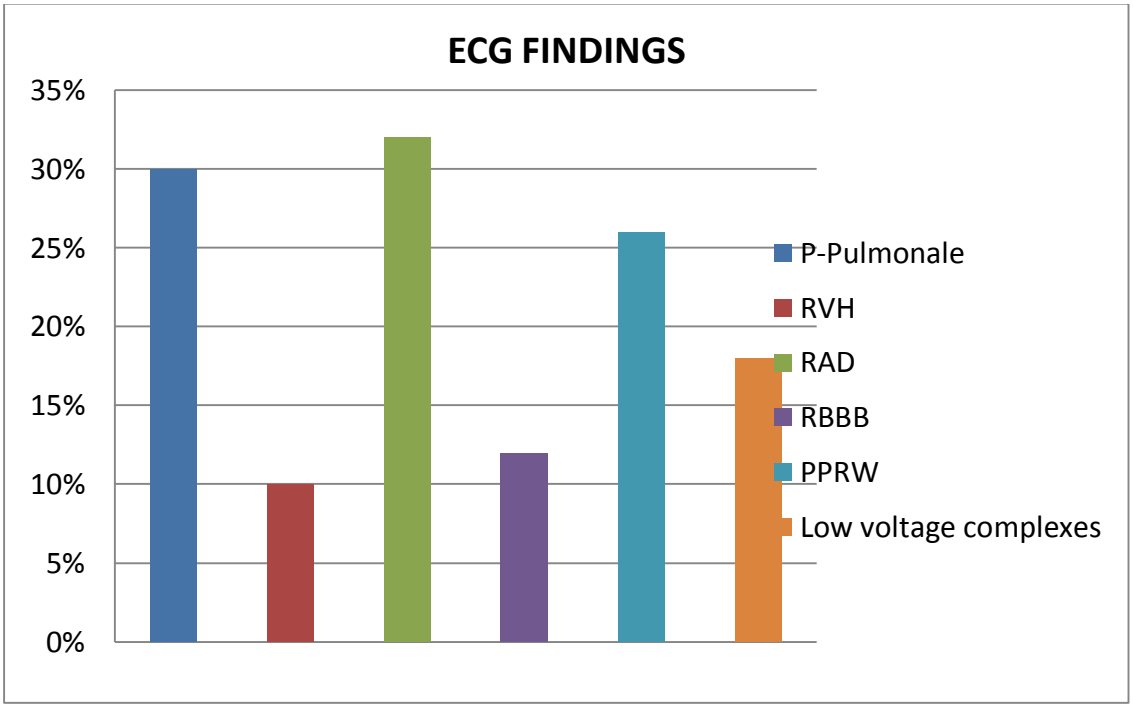


Table 8. ECHO Findings

ECHO findings	Frequency	Percent
LV SYSTOLIC DYSFUNTION	6	6.0%
LV DIASTOLIC DYFUNCTION	80	80.0%
PULMONARY HYPERTENSION	50	50.0%
DILATED RA/RV	30	30.0%
RV DYSFUNCTION	14	14.0%

In our study, most common Echo finding is Left Ventricular Diastolic dysfunction, seen in 80% of patients. 50% patients had Pulmonary Hypertension. Dilated Right Atrium and Ventricle seen in 30% of patients. Right Ventricular Dysfunction seen in 14% of Patients. Left Ventricular Systolic Dysfunction seen in 6% of patients.

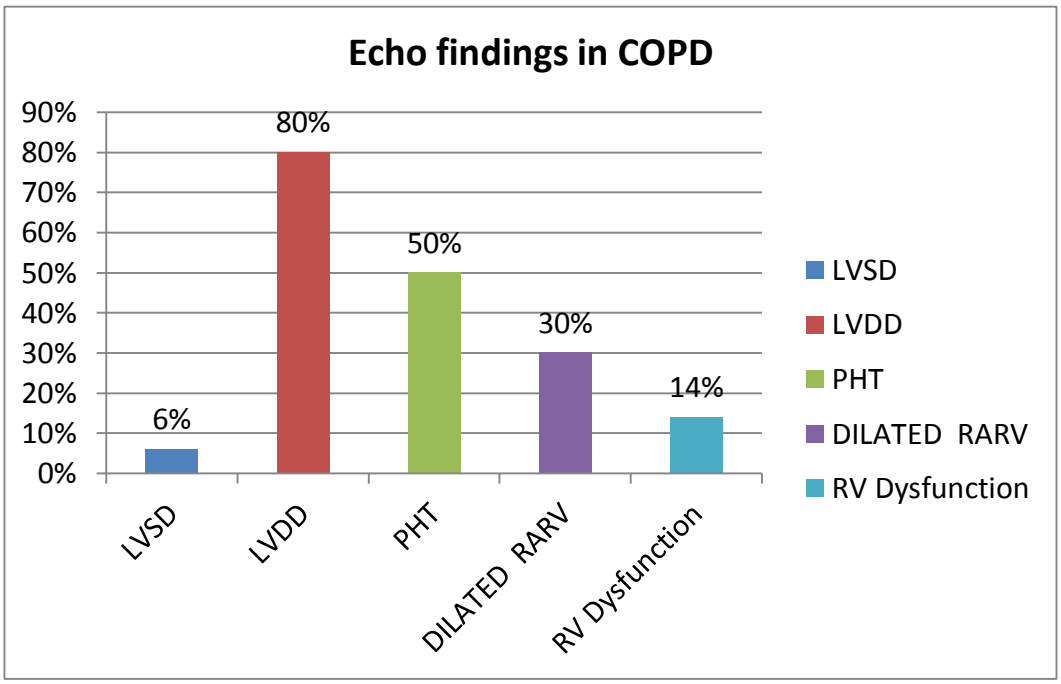
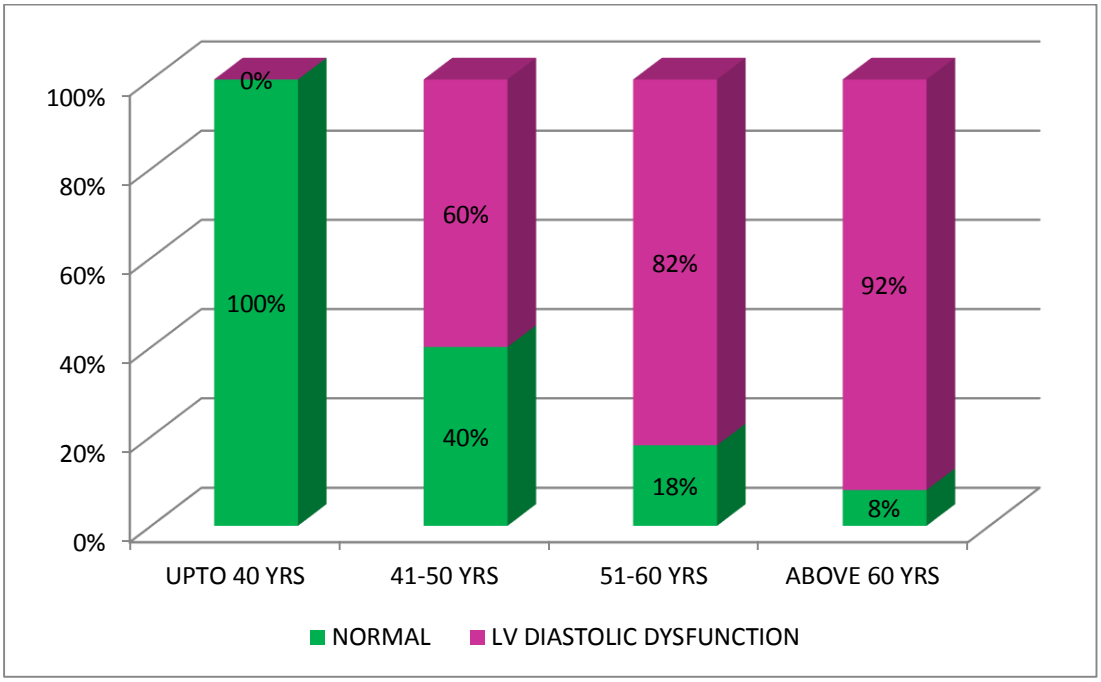


Table 9. Correlation between Patient's Age and LV Diastolic Dysfunction

Age group	No. patients	LV Diastolic Dysfunction	Chi square	P value
Upto 40 yrs	2	0	16.795*	P<0.001
41-50 yrs	20	12		
51-60 yrs	39	32		
Above 60 yrs	39	36		
Total	100	80		

CORRELATION COEFFICIENT r =0.373*

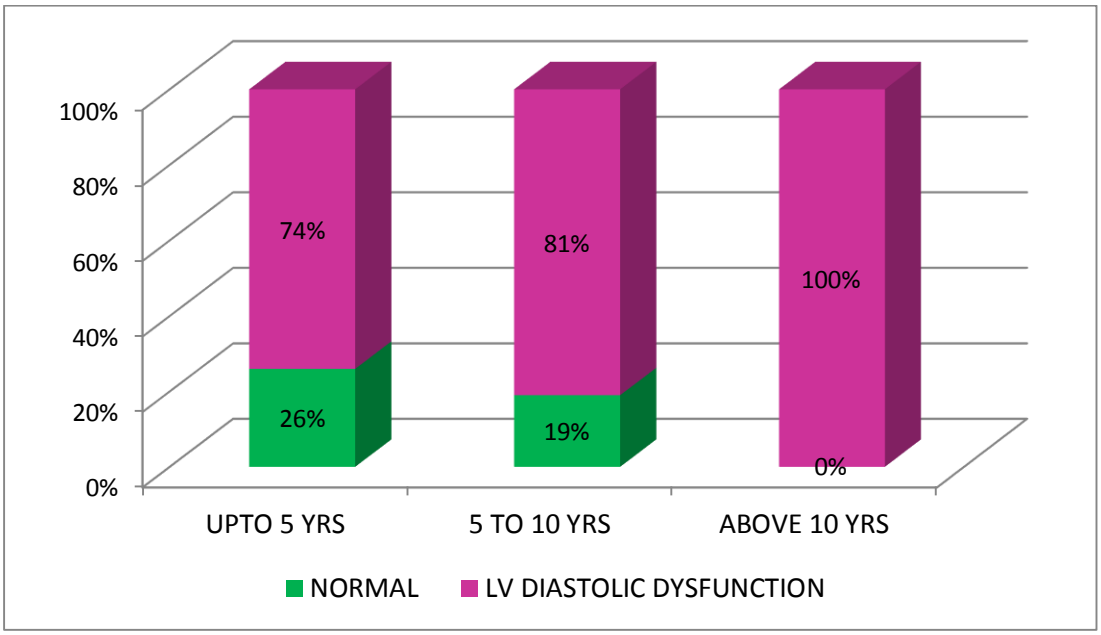


In our study, there is high prevalence of Left Ventricular diastolic dysfunction seen in patients above 60 years of age (92%). As age advances, prevalence of LV diastolic dysfunction increases.

Table 10. Correlation between duration of symptoms and LV Diastolic Dysfunction

Duration of symptoms	No patients	LV diastolic dysfunction	Chi square	P value
Upto 5 yrs	54	40	4.238*	0.038
5-10	32	26		
Above 10 yrs	14	14		
Total	100	80		

CORRELATION COEFFICIENT r =0.208*

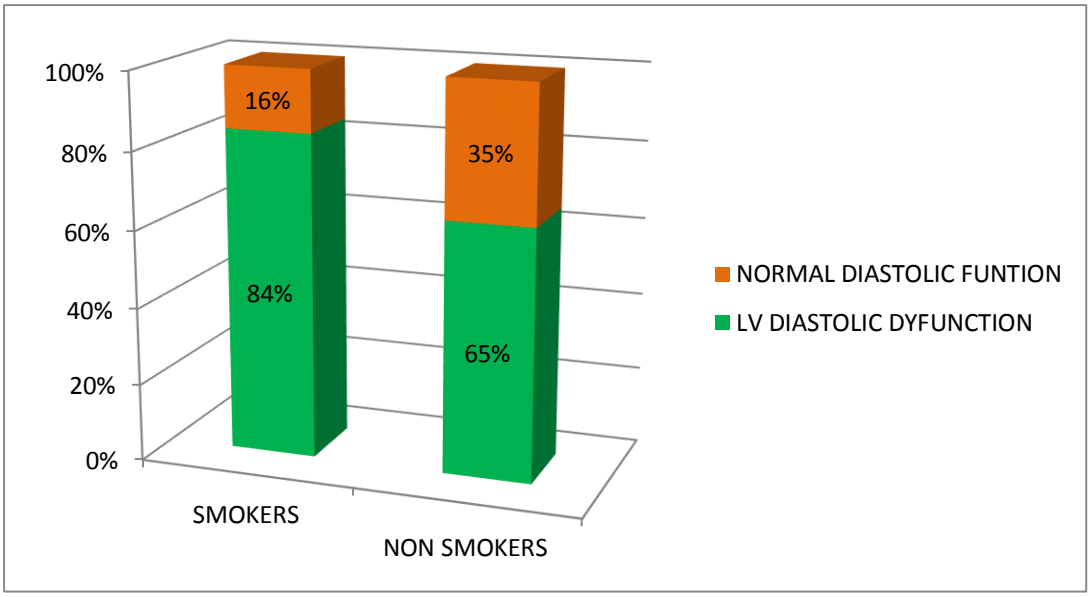


In this study, prevalence of LV diastolic dysfunction increases when duration of symptoms increases. Patients with duration of symptoms above 10 years universally all had LV diastolic dysfunction. But patient with less years of symptoms also had high prevalence of LV diastolic dysfunction.

Table 11. Correlation between smoking status and LV Diastolic Dysfunction

	No. patients	LV Diastolic Dysfunction	Chi square	P value
NON SMOKERS	23	15	4.080*	P<0.05
SMOKERS	77	65		
Total	100	80		

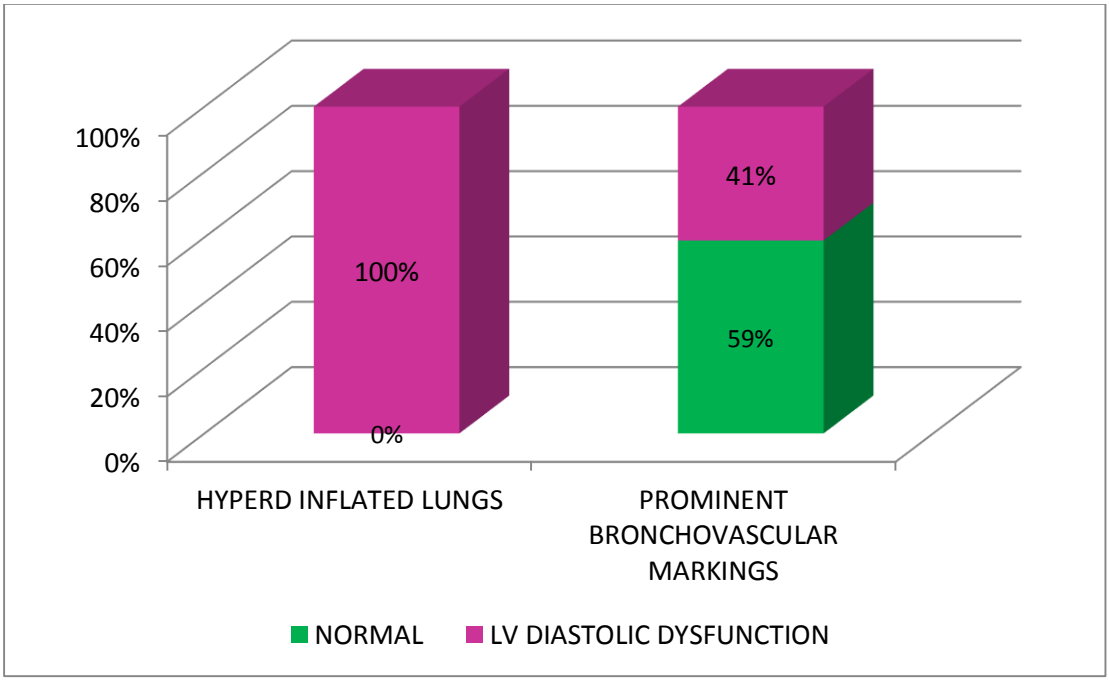
CORRELATION COEFFICIENT r =0.202*



In this study, LV diastolic dysfunction had been seen in both smokers and smokers. But smokers had high prevalence of LV diastolic dysfunction compared to non-smokers.

Table 12. Correlation between Chest X ray findings and LV diastolic dysfunction

Chest X ray signs	No. Patients	LV diastolic dysfunction	Chi square	P value
Hyper inflation	66	66	48.529*	P<0.001
Prominent Bronchovasucular markings	34	14		
Total	100	80		

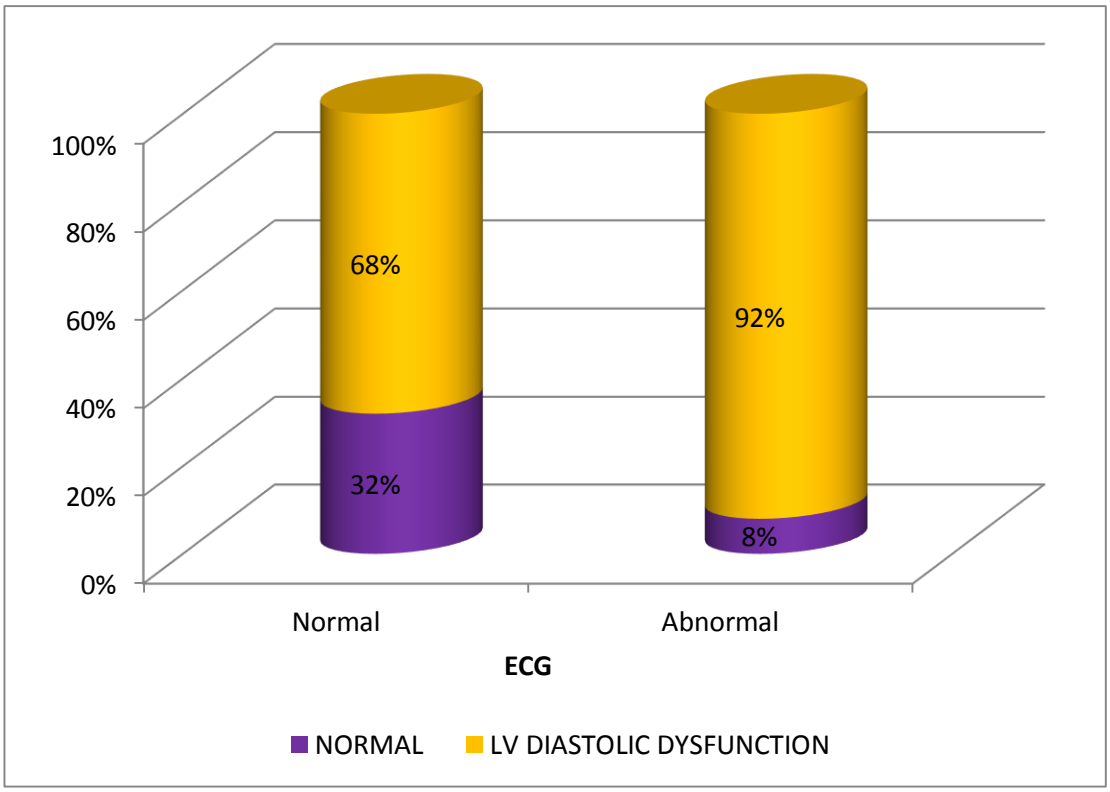


In our study, all patients with hyperinflated lungs on imaging had LV diastolic dysfunction (100%). 41% of patients with prominent bronchovascular markings on chest x ray had LV diastolic dysfunction.

Table 13. Correlation between ECG findings and LV diastolic dysfunction

	No. Patients	LV Diastolic Dysfunction	Chi square	P value
Normal ECG	50	34	9.00	0.003
Abnormal ECG	50	46		
Total	100	80		

CORRELATION COEFFICIENT r = 0.300*



In this study, 50% of patients had normal ECG finding and 50% had ECG changes of COPD. Patients with abnormal ECG had high prevalence of LV diastolic dysfunction (92%) compared to normal ECG (68%). This study shows that LV diastolic dysfunction can occur even in the absence of ECG findings of COPD.

Table 14. Correlation between Stages of COPD and grading of LV diastolic dysfunction

Stage of COPD	No. Patients	Grading of LV Diastolic Dysfunction				Chi square	P value
		I	II	III	IV		
I	16	2	0	0	0	112.175	P < 0.001
II	40	34	0	0	0		
III	30	22	8	0	0		
IV	14	2	8	4	0		
Total	100	60	16	4	0		

CORRELATION COEFFICIENT r = 0.791*

In our study, Among 16 stage I COPD patients, only 2 were had grade I LV diastolic dysfunction, others had normal diastolic function. Among 40 stage II patients, 34 had grade I diastolic dysfunction. In 30 stage III patients, 22 had grade I and 8 had grade II diastolic

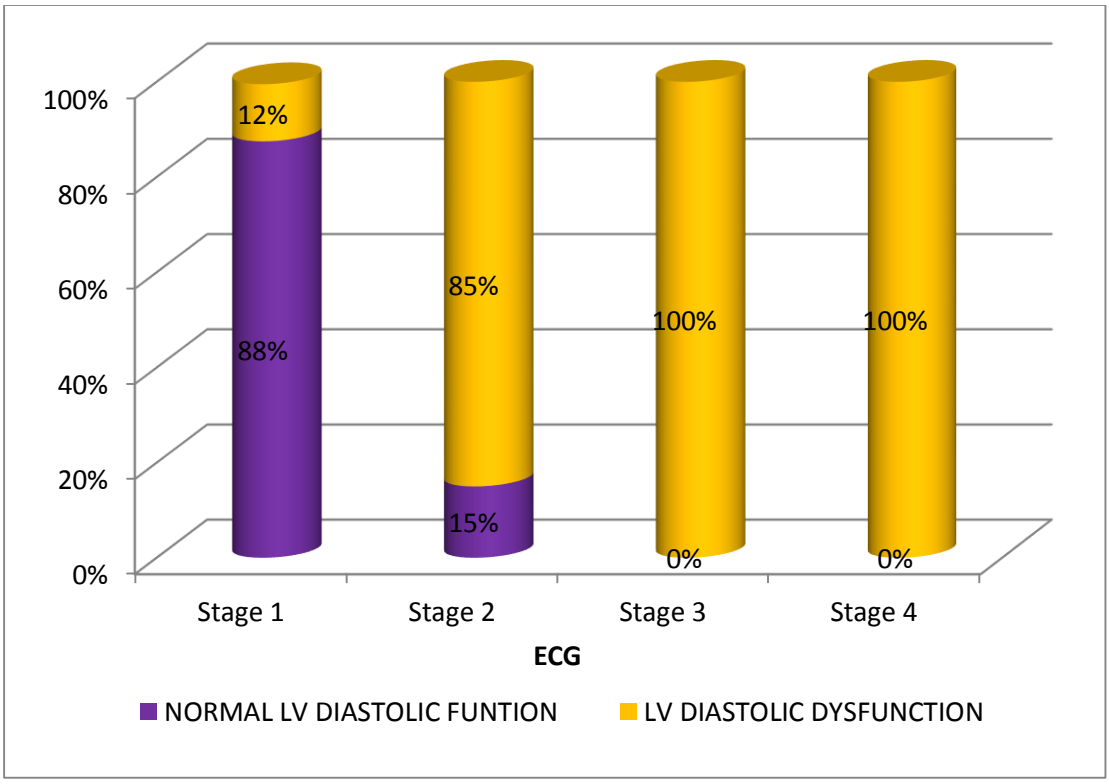
dysfunction. In 14 stage IV patients, 2 patients had grade I, 8 patients had grade II and 4 patients had grade III LV diastolic dysfunction. There was significant correlation between stage of COPD and grading of LV diastolic dysfunction.

Table 15. Correlation between with GOLD staging and LV diastolic dysfunction

Gold Stage of COPD	No. Patients	LV Diastolic dysfunction	Chi square	P value
I	16	2	57.188	P<0.001
II	40	34		
III	30	30		
IV	14	14		
Total	100	80		

CORRELATION COEFFICIENT r = 0.610*

In this study, among 100 patients, 80 had LV diastolic dysfunction. In stage I among 16 patients only 2 had diastolic dysfunction (12%). In stage II, among 40 patients 34 had LV diastolic dysfunction (88%). In stage III and IV all patients had LV diastolic dysfunction (100%). There was significant correlation between stages of COPD and left ventricular diastolic dysfunction.


100%
80%
60%
40%
20%
0%
12%
88%
85%
15%
100%
0%
100%
0%
Stage 1
Stage 2
Stage 3
Stage 4
ECG
NORMAL LV DIASTOLIC FUNTION
LV DIASTOLIC DYSFUNCTION

DISCUSSION

DISCUSSION

Our study was conducted in patients with chronic obstructive pulmonary disease to know the prevalence of left ventricular diastolic dysfunction. Our study population included 100 patients who were diagnosed as chronic obstructive pulmonary disease by clinical, imaging and pulmonary function test. All 100 patients were evaluated for cardiac status by electrocardiography and echocardiography and were screened for left ventricular diastolic dysfunction. Analysis was made to study the correlation between GOLD stages COPD and prevalence of left ventricular diastolic dysfunction by using Chi-square test. Following were the observations made from our study in COPD patients

Age distribution:

Out of 100 patients, majority of patients were in the age group of above 50 years (78%). Only two cases were seen below 40 years. This showed that COPD is the disease occurs after 40 years of age.

Sex distribution:

Out of 100 patients in this study, 81 patients were male, 19 patients were female. Male to female ratio 4:1

Duration of symptoms:

In this study, majority of patients had duration of symptoms less than 5 years (54%). Duration of symptoms more than 10 years was less frequent (14%)

Smoking status:

Out of 100 patients, 77 patients were smokers and 23 patients were nonsmokers. This showed that smoking is the main risk factor for chronic obstructive pulmonary disease. So the disease is common in males.

Stage of COPD:

In our study, patients were staged according to GOLD classification. Spirometry was used to assess the stage. Stages were based on post bronchodilator FEV_1. 16 patients were in stage I (16%), 40 patients were in Stage II (40%), 30 patients were in stage III (30%), 14 patients were in stage IV (14%). Majority of patients were in Stage II & III. 56 patients were in early stages (I&II), 44 patients were in late stages (III & IV).

Chest X findings:

Most common radiological finding in our study is hyperinflated lung fields, which is seen in 66% of patients. Prominent bronchovascular markings were seen in 34 patients. In this study, emphysematous lungs were more common than chronic bronchitis.

ECG findings:

Out 100 patients in our study, 50 patients ECG were with in normal limits. 50 patients ECG showed signs of chronic obstructive pulmonary disease. Most common ECG findings were right axis deviation and P-Pulmonale (RAD – 32%, P-Pulmonale - 30%). Next common findings were poor progression of R wave (26%) and low voltage compexes (18%). RVH pattern was seen only in 10% of patients. This showed that ECG findings can be normal in COPD patients with Pulmonary hypertension.

Echocardiographic findings:

Most common echo finding among 100 patiens was Left ventricular diastolic dysfunction. 80% of patients had left diastolic dysfunction. 50% of patients had Pulmonary hypertension. RV

dysfunction was seen in 14% patients and LV systolic dysfunction was seen in 6% of patients.

LV diastolic function was assessed and graded by Doppler echocardiography. Most of the patients had grade I diastolic dysfunction (60%). 16 patients had grade II diastolic dysfunction (16%) and 4 patients had grade III diastolic dysfunction (4%)

LV Diastolic dysfunction and COPD:

Our study showed that there is high prevalence of Left Ventricular diastolic dysfunction in chronic obstructive pulmonary disease and there is close association between and LV diastolic dysfunction and severity of COPD. LV diastolic dysfunction can also occur in early stages (Stage I and II) of COPD. This study showed that most of the patient with stage II had mild left diastolic dysfunction. In later stages (III&IV), all patients had left ventricular diastolic dysfunction and severity of dysfunction also increases. So this study showed that there is significant correlation between prevalence of LV diastolic dysfunction and severity of COPD.

LV diastolic dysfunction can occur in COPD patients irrespective of age, sex, duration of symptoms and smoking status. This also showed that LV diastolic dysfunction can occur even the absence of Pulmonary

Hypertension and significant changes in ECG and chest X ray. The study "Prevalence of Left Ventricular diastolic dysfunction in COPD" was comparable to studies conducted by Caram LM et al[93], Boussuges et al[94], Rutten et al[95], and Funk et al[77], Godoy et al.[97]

In agreement with our results, Caram LM et al. showed high prevalence of LV diastolic function (88%) in COPD and it is associated with disease severity.[93]

Boussuges et al. found a high prevalence of left ventricular diastolic dysfunction in COPD (76%) compared to control (35%)[94]. Rutten et al. and Funk et al. also reported the prevalence above 50%.

In agreement with our results Godoy et al. showed higher prevalence of LVDD among COPD patients which is associated with increased disease severity, and the prevalence was 88%[97]

. Other factors influence the development of LV diastolic dysfunction are

- Age
- Smoking
- Duration of symptoms

Age:

This study showed that, As the age advances, prevalence of LV diastolic dysfunction also increases. So LV diastolic dysfunction was more common in older individuals compare to younger individuals. This correlation was observed in Ying sum et al. [83]

Smoking:

Our study showed that LV diastolic dysfunction can occur even in the absence of smoking history. But our study also showed that smoking significantly increase the risk of developing LV diastolic dysfunction as earlier due to rapid decline in $FEV_{1.}$

Duration of symptoms:

This study showed that Duration of symptoms and disease also significantly affects the development of LV diastolic dysfunction. As the duration of symptoms increases, prevalence of diastolic dysfunction increases.

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CONCLUSION

CONCLUSION

Following results were concluded from our study:

- Chronic obstructive pulmonary disease was more commonly seen in middle aged patients and rare below the age of 35 years and is common in males than females with male to female ratio 4:1
- Smoking was the main risk factor for COPD
- Majority of the patients are in GOLD stage II
- Most common chest X ray finding was hyper inflated lung fields
- Half of patients had normal ECG findings
- Right axis deviation and P-Pulmonale were the common ECG findings
- Mild LV diastolic dysfunction was the most common Echo finding
- There was high prevalence of Left Ventricular diastolic dysfunction in COPD patients.

- LV diastolic dysfunction can be present even in the absence of pulmonary hypertension and it can be observed in early stages of COPD.

- LV diastolic dysfunction can occur even in the absence of significant changes in ECG.

- Significant correlation was observed between LV diastolic dysfunction and Age of the patients, smoking status, duration of symptoms.

- There is definite statistical correlation between LV diastolic dysfunction and severity of COPD

SUMMARY

SUMMARY

COPD is a systemic disease and frequently co-exists with cardiovascular complications. Left ventricular diastolic dysfunction is one of the common cardiac manifestation, highly prevalent in COPD patients, which significantly affects the morbidity and mortality

Left diastolic dysfunction can be asymptomatic or associated with heart failure symptoms. Often diastolic heart failure coexists with acute exacerbation of COPD and it is very difficult to diagnose and it challenges the managing physicians. It is very important to exclude decompensated heart failure during COPD exacerbation.

All patients with COPD should undergo cardiac evaluation by echocardiography particularly to assess the LV diastolic function and diastolic heart failure can be managed with Cardioselective Beta blockers, ACE inhibitors and Diuretics.

All patients should be educated about Pulmonary Rehabilitation Programme including exercise training and smoking cessation, which improves the survival of the patient and significantly reduce the co morbidities associated with COPD.

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ANNEXURE

PREVALENCE OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

PROFORMA

Name :

Age:

Sex:

Address:

Occupation:

Duration of disease:

Presenting complaints:

Past history:

- Diabetes Mellitus
- Hypertension
- Heart Diseases
- Chronic Kidney Disease

Smoking history:

Smoking duration:

Pack years:

General Examination

- Built
- Nourishment
- Height
- Weight
- Pallor
- Icterus
- Clubbing
- Cyanosis
- Pedal edema
- Lymphadenopathy
- Jugular venous pulse

VITALS SIGNS:

PR -
BP -
RR -

SYSTEMIC EXAMINATION

RS Examination:

CVS Examination:

Per Abdomen:

CNS Examination:

INVESTIGATIONS

Chest X ray:

- Hyperinflated lung fields
- Prominent Bronchovascular markings

Electrocardiography:

- P-Pulmonale
- Right Axis Deviation
- Right Ventricular Hypertrophy
- Right Bundle Branch Block
- Poor Progression of R wave
- Low voltage complexes
- Arrhythmias

Pulmonary Function Test:

FEV_1:
FVC:
FEV_1/FVC:
Stage of COPD:

Echocardiography:

LV systolic Function:
LV Diastolic Function:
Pulmonary Hypertension:
Dilated RA/RV:
RV dysfunction:

INFORMATION SHEET

We are conducting a study on **"STUDY ON PREVALENCE OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE"** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to identify Left ventricular diastolic dysfunction in COPD patients.

We are selecting certain patients with CHRONIC OBSTRUCTIVE PULMONARY DISEASE who are found eligible, and the patients are subjected to special tests ELECTROCARDIOGRAM, ECHOCARDIOGRAM, SPIROMETRY, which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of the Participant

Date:

Place:

PATIENT CONSENT FORM

Study Detail	:	**Study on Prevalence of Left ventricular diastolic dysfunction in Chronic Obstructive Pulmonary Disease**
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.

Signature/thumb impression
Patient's Name and Address:

Signature of the investigator
Study investigator's name

ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜிவ் காந்தி அரசு பொது மருத்துவமனையில் அனுமதிக்கப்படும் நாள்பட்ட நுரையீரல் அடைப்பு நோயினைப் பற்றிய ஒரு ஆராய்ச்சி நடைபெற்று வருகிறது.

நாள்பட்ட நுரையீரல் அடைப்பு நோயினால் இதயத்தின் இடது வெண்ட்ரிக்கிளில் விரிவியக்க பிறழ்ச்சி ஏற்படுவதை மின் ஒலி இதைய வரைவு மூலம் அறிவதை இந்த ஆராய்ச்சியின் நோக்கமாகும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்சிசியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு:

நாள்பட்ட நுரையீரல் அடைப்பு நோயினால் இதயத்தின் இடது வென்ட்ரிக்கிளில் விரிவியக்க பிறழ்ச்சி ஏற்படுவதை பற்றிய ஆராயச்சி.

பெயர்: தேதி:

வயது: உள்நோயாளி எண்:

பால்: ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்ப்பேரில் பங்கு பெறுகிறேன். இந்த ஆராய்ச்சியில் இருந்து நான் எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்து கொண்டேன்.

நான் இந்த ஆராய்ச்சியின் விபரங்களைக்கொண்ட ஆராய்ச்சி தகவல் தாளை பெற்றுக்கொண்டேன்.

இதன் மூலம் எந்த பின் விளைவும் ஏற்படாது என்று மருத்துவர் மூலம் தெரிந்துக்கொண்டு இந்த மருத்துவ ஆராய்ச்சியில் என்னனை சேர்த்துக்கொள்ள சம்மதம் தெரிவிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்ப்பாளர் கையொப்பம்

நாள்:
இடம்:

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.B.Sivasubramanian
Postgradaute M.D.(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.B.Sivasubramanian,

The Institutional Ethics Committee has considered your request and approved your study titled **"Study on prevalence of left ventricular diastolic dysfunction in Chronic Obstructive Pulmonary Disease" No.11052015.**

The following members of Ethics Committee were present in the meeting held on 12.05.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S., Professor of Surgery, MMC	: Member
6. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
7. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
8. Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
9. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
10. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

23/6/15

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

KEY TO MASTER CHART

A – Absent

ECG – Electrocardiogram

F – Female

FEV_1 – Forced Expiratory Volume in one second

FVC – Forced Vital Capacity

LVDD – Left ventricular diastolic dysfunction

LVSD – Left ventricular systolic dysfunction

M – Male

P – Present

PFT – Pulmonary Function Test

PHT – Pulmonary hypertension

PPRW – Poor Progression of R wave

RA – Right Atrium

RAD – Right axis deviation

RBBB – Right Bundle Branch Block

RV – Right Ventricle

RVH – Right Ventricular Hypertrophy

RVH – Right Ventricular Hypertrophy

MASTER CHART

MASTER CHART

S.No	Age	sex	IP. No.	Smoking (Pack Years)	Duration of Symptoms (years)	PFT		Stage of COPD (Gold)	Chest X ray		ECG						ECHO				
						FEV1/FVC	FEV1		Hyper Inflation	Prominent Bronchovascular markings	P-Pulmonale	RVH	RAD	RBBB	PPRW	Low voltage complexes	LVSD	LVDD (Grading)	PHT	Dilated RA/RV	RV Dysfunction
1	55	M	49012	15	8	<0.7	47	III	P	A	P	A	P	A	A	A	A	II	P	P	A
2	49	M	56897	10	3	<0.7	55	II	P	A	A	A	A	A	A	A	A	I	A	A	A
3	62	M	54321	12	2	<0.7	65	II	P	A	A	A	A	P	P	A	A	I	P	A	A
4	48	M	50098	9	1	<0.7	83	I	A	P	A	A	A	A	A	A	A	A	A	A	A
5	62	F	55471	0	4	<0.7	75	II	P	A	A	A	A	A	P	P	A	I	P	A	A
6	69	M	57912	16	12	<0.7	27	IV	P	A	P	A	P	A	P	A	P	III	P	P	P
7	51	M	56823	11	6	<0.7	59	II	A	P	A	A	A	A	A	A	A	I	A	A	A
8	54	F	59864	0	9	<0.7	41	III	A	P	P	P	P	A	A	A	A	I	P	P	A
9	65	M	58734	17	7	<0.7	36	III	P	A	A	A	P	P	P	P	A	I	A	A	A
10	57	M	57908	22	13	<0.7	28	IV	P	A	P	P	P	A	A	A	A	II	P	P	P
11	45	M	57143	5	2	<0.7	75	II	A	P	A	A	A	A	A	A	A	A	A	A	A
12	70	M	55876	20	15	<0.7	40	III	P	A	A	A	A	A	P	P	A	II	P	P	A
13	52	F	56002	0	7	<0.7	85	I	A	P	A	A	A	A	A	A	A	A	A	A	A
14	58	M	56405	10	3	<0.7	83	I	A	P	A	A	A	A	A	A	A	A	A	A	A
15	65	M	50834	16	7	<0.7	29	IV	P	A	P	A	P	P	P	A	A	I	P	P	P
16	67	M	51890	12	9	<0.7	61	II	P	A	A	A	P	A	A	A	A	I	A	A	A

17	51	M	52675	6	1	<0.7	70	II	P	A	A	A	A	A	A	A	A	I	A	A	A
18	59	M	53097	11	4	<0.7	48	III	A	P	P	A	P	A	A	A	A	I	P	P	A
19	65	M	54771	9	7	<0.7	34	III	P	A	A	A	A	A	A	A	A	II	P	A	A
20	61	M	58234	10	4	<0.7	57	II	P	A	A	A	A	A	A	A	A	I	A	A	A
21	67	F	60932	0	6	<0.7	42	III	P	A	P	A	P	P	P	P	A	I	P	A	A
22	54	M	61234	7	2	<0.7	67	II	A	P	A	A	A	A	P	A	A	I	A	A	A
23	55	M	60456	9	1	<0.7	76	II	P	A	P	P	A	A	A	A	A	I	P	A	A
24	70	M	61935	21	4	<0.7	26	IV	P	A	P	A	P	A	P	P	A	III	P	P	P
25	59	M	59006	14	3	<0.7	85	I	P	A	A	A	A	A	A	A	A	I	A	A	A
26	72	F	56456	0	8	<0.7	40	III	P	A	A	A	A	A	P	P	P	II	P	A	A
27	53	M	62345	20	5	<0.7	59	II	P	A	A	A	A	A	A	A	A	I	A	A	A
28	64	M	66879	11	12	<0.7	33	III	P	A	A	A	A	A	A	A	A	I	A	A	A
29	49	M	65106	7	6	<0.7	61	II	A	P	P	A	P	A	A	A	A	A	P	P	A
30	60	F	66479	0	2	<0.7	89	I	A	P	A	A	A	A	A	A	A	A	A	A	A
31	45	M	59487	10	3	<0.7	39	III	P	A	P	A	P	A	A	A	A	I	P	P	A
32	47	M	58146	7	5	<0.7	76	II	P	A	A	A	A	A	A	A	A	I	A	A	A
33	55	M	64501	10	4	<0.7	67	II	A	P	A	A	A	A	A	A	A	I	A	A	A
34	46	M	66305	5	2	<0.7	89	I	A	P	A	A	A	A	A	A	A	A	A	A	A
35	50	F	62348	0	5	<0.7	41	III	P	A	A	A	A	A	P	P	A	I	P	A	A
36	71	M	63209	25	15	<0.7	28	IV	P	A	P	P	P	A	A	A	P	II	P	P	P
37	65	M	64025	18	12	<0.7	25	IV	P	A	P	A	P	P	P	P	A	II	P	P	P
38	59	M	65754	11	9	<0.7	74	II	A	P	A	A	P	A	A	A	A	A	P	A	A
39	58	F	70001	0	8	<0.7	47	III	P	A	A	A	A	A	A	A	A	I	P	A	A
40	43	M	69806	7	3	<0.7	68	II	A	P	A	A	A	A	A	A	A	I	A	A	A
41	68	M	60407	0	3	<0.7	85	I	A	P	A	A	A	A	A	A	A	A	A	A	A
42	39	M	68900	0	1	<0.7	84	I	A	P	A	A	A	A	A	A	A	A	A	A	A
43	44	M	67608	12	2	<0.7	67	II	P	A	A	A	A	A	A	A	A	I	A	A	A
44	59	F	67100	0	13	<0.7	29	IV	P	A	P	P	P	A	A	A	A	II	P	P	P
45	65	M	68340	15	8	<0.7	71	II	P	A	A	A	A	A	A	A	A	I	A	A	A
46	57	M	68934	12	5	<0.7	40	III	P	A	A	A	A	A	A	A	A	I	A	A	A

47	53	M	69403	8	4	<0.7	39	III	P	A	P	A	A	P	A	A	A	I	P	P	A
48	68	M	70265	9	10	<0.7	73	II	A	P	A	A	A	A	A	A	A	I	A	A	A
49	70	M	70864	15	7	<0.7	70	II	P	A	A	A	A	A	A	A	A	I	P	P	A
50	53	F	63786	0	3	<0.7	43	III	P	A	A	A	A	A	P	P	A	I	P	A	A
51	46	M	71200	5	2	<0.7	75	II	A	P	A	A	A	A	A	A	A	A	A	A	A
52	71	M	71508	20	15	<0.7	40	III	P	A	A	A	A	A	P	P	P	II	P	P	A
53	51	F	71945	0	7	<0.7	85	I	A	P	A	A	A	A	A	A	A	A	A	A	A
54	59	M	73206	11	3	<0.7	83	I	A	P	A	A	A	A	A	A	A	A	A	A	A
55	66	M	73145	15	7	<0.7	29	IV	P	A	P	A	P	P	P	A	A	I	P	P	P
56	68	F	73897	0	6	<0.7	42	III	P	A	P	A	P	P	P	P	A	I	P	A	A
57	55	M	73502	8	2	<0.7	67	II	A	P	A	A	A	A	P	A	A	I	A	A	A
58	54	M	72845	10	1	<0.7	76	II	P	A	P	P	A	A	A	A	A	I	P	A	A
59	71	M	72108	20	4	<0.7	26	IV	P	A	P	A	P	A	P	P	A	III	P	P	P
60	58	M	72765	15	3	<0.7	85	I	P	A	A	A	A	A	A	A	A	I	A	A	A
61	46	M	74002	9	3	<0.7	39	III	P	A	P	A	P	A	A	A	A	I	P	P	A
62	48	M	74354	7	5	<0.7	76	II	P	A	A	A	A	A	A	A	A	I	A	A	A
63	54	M	74634	11	4	<0.7	67	II	A	P	A	A	A	A	A	A	A	I	A	A	A
64	49	M	75102	6	2	<0.7	89	I	A	P	A	A	A	A	A	A	A	A	A	A	A
65	51	F	75492	0	5	<0.7	41	III	P	A	A	A	A	A	P	P	A	I	P	A	A
66	69	M	76546	0	3	<0.7	85	I	A	P	A	A	A	A	A	A	A	A	A	A	A
67	40	M	77095	0	1	<0.7	84	I	A	P	A	A	A	A	A	A	A	A	A	A	A
68	43	M	77234	11	2	<0.7	67	II	P	A	A	A	A	A	A	A	A	I	A	A	A
69	59	F	77850	0	13	<0.7	29	IV	P	A	P	P	P	A	A	A	A	II	P	P	P
70	64	M	76098	14	8	<0.7	71	II	P	A	A	A	A	A	A	A	A	I	A	A	A
71	56	M	76438	16	8	<0.7	48	III	P	A	P	A	P	A	A	A	A	II	P	P	A
72	48	M	78609	12	3	<0.7	56	II	P	A	A	A	A	A	A	A	A	I	A	A	A
73	61	M	79256	11	2	<0.7	65	II	P	A	A	A	A	P	P	A	A	I	P	A	A
74	49	M	79699	8	1	<0.7	82	I	A	P	A	A	A	A	A	A	A	A	A	A	A
75	63	F	74687	0	4	<0.7	74	II	P	A	A	A	A	A	P	P	A	I	P	A	A
76	72	M	71204	24	15	<0.7	29	IV	P	A	P	P	P	A	A	A	P	II	P	P	P

77	66	M	80789	19	12	<0.7	26	IV	P	A	P	A	P	P	P	P	A	II	P	P	P
78	58	M	80384	12	9	<0.7	73	II	A	P	A	A	P	A	A	A	A	A	P	A	A
79	59	M	80408	13	8	<0.7	48	III	P	A	A	A	A	A	A	A	A	I	P	A	A
80	44	F	80957	0	3	<0.7	69	II	A	P	A	A	A	A	A	A	A	I	A	A	A
81	58	M	81209	11	5	<0.7	41	III	P	A	A	A	A	A	A	A	A	I	A	A	A
82	54	M	81606	9	4	<0.7	38	III	P	A	P	A	A	P	A	A	A	I	P	P	A
83	69	M	81456	10	10	<0.7	72	II	A	P	A	A	A	A	A	A	A	I	A	A	A
84	71	M	82345	16	7	<0.7	69	II	P	A	A	A	A	A	A	A	A	I	P	P	A
85	54	M	82609	17	3	<0.7	44	III	P	A	A	A	A	A	P	P	A	I	P	A	A
86	68	M	82991	15	12	<0.7	28	IV	P	A	P	A	P	A	P	A	P	III	P	P	P
87	50	M	83035	13	6	<0.7	58	II	A	P	A	A	A	A	A	A	A	I	A	A	A
88	53	F	83789	0	9	<0.7	42	III	A	P	P	P	P	A	A	A	A	I	P	P	A
89	66	M	83125	16	7	<0.7	35	III	P	A	A	A	P	P	P	P	A	I	A	A	A
90	58	M	84687	23	13	<0.7	27	IV	P	A	P	P	P	A	A	A	A	II	P	P	P
91	68	M	84890	14	9	<0.7	60	II	P	A	A	A	P	A	A	A	A	I	A	A	A
92	52	M	85209	7	1	<0.7	69	II	P	A	A	A	A	A	A	A	A	I	A	A	A
93	58	F	85867	0	4	<0.7	49	III	A	P	P	A	P	A	A	A	A	I	P	P	A
94	64	M	86239	8	7	<0.7	35	III	P	A	A	A	A	A	A	A	A	II	P	A	A
95	62	M	86098	11	4	<0.7	58	II	P	A	A	A	A	A	A	A	A	I	A	A	A
96	71	M	87781	16	8	<0.7	41	III	P	A	A	A	A	A	P	P	A	II	P	A	A
97	54	M	89004	21	5	<0.7	68	II	P	A	A	A	A	A	A	A	A	I	A	A	A
98	65	M	76662	12	12	<0.7	32	III	P	A	A	A	A	A	A	A	A	I	A	A	A
99	48	M	90823	8	6	<0.7	60	II	A	P	P	A	P	A	A	A	A	A	P	P	A
100	61	F	74567	0	2	<0.7	88	I	A	P	A	A	A	A	A	A	A	A	A	A	A

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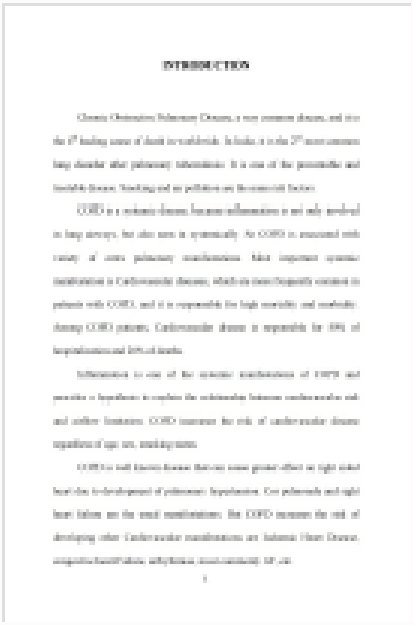

INTRODUCTION


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INTRODUCTION
Chronic Obstructive Pulmonary Disease, a very common disease, and it is the 4th leading cause of death in worldwide. In India, it is the 2nd most common lung disorder after pulmonary tuberculosis. It is one of the preventable and treatable disease. Smoking and air pollution are the main risk factors.
COPD is a systemic disease, because inflammation is not only involved in lung airways, but also seen in systemically. So COPD is associated with variety of extra pulmonary manifestations. Most important systemic manifestation is Cardiovascular diseases, which are more frequently common in patients with COPD, and it is responsible for high mortality and morbidity. Among COPD patients, Cardiovascular disease is responsible for 50% of hospitalization and 20% of deaths.
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